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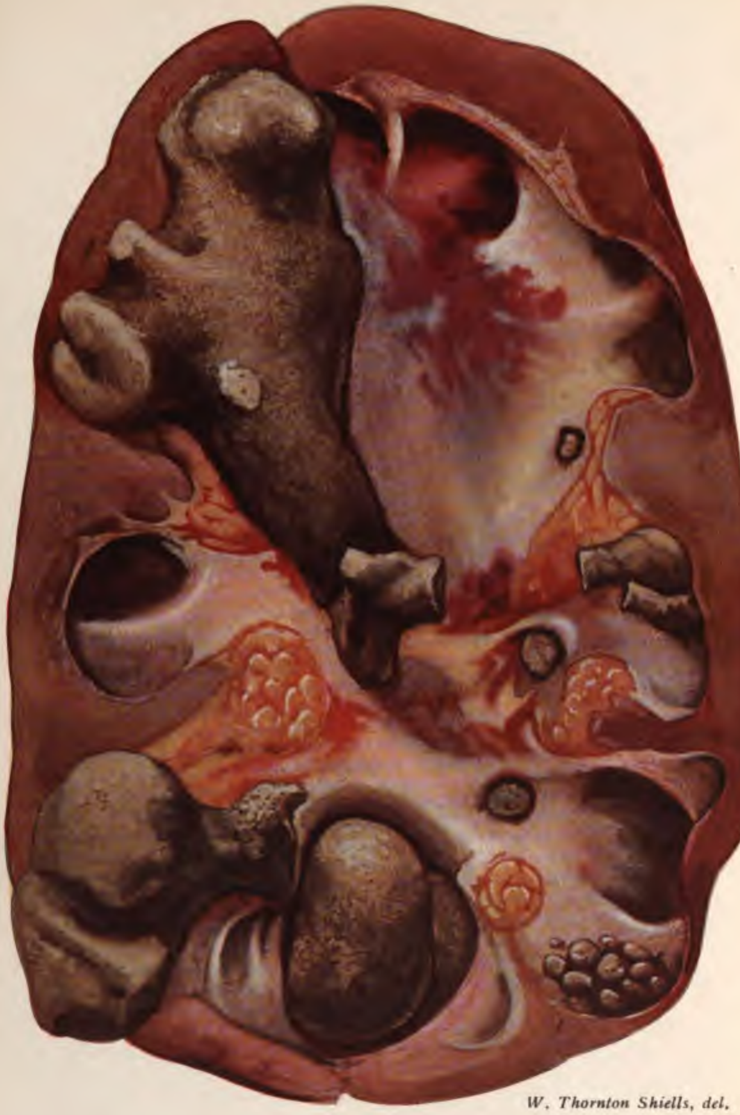

Calculous disease of the Kidney. Nephrectomy
(author's case).

ESTIMATION OF THE RENAL FUNCTION IN URINARY SURGERY

BY

J. W. THOMSON WALKER

M.B., C.M. (EDIN.), F.R.C.S.

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ESTIMATION OF THE RENAL FUNCTION IN URINARY SURGERY

BY

J. W. THOMSON WALKER
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WITH 2 COLOURED AND 7 BLACK-AND-WHITE PLATES
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PREFACE

Of recent years Surgery has drawn closer to the fundamental sciences of Pathology and Physiology in the search for information that will give increased accuracy in diagnosis and ensure greater safety in operation.

In the following pages will be found a clinical study of the present means of estimating the renal function in surgical diseases of the urinary organs which involves a study of symptomatology and of the application of physiological methods to diagnosis in urinary surgery. To this is added some discussion of the cases to which such methods are applicable.

The signs of a failing renal function are usually insignificant, and constant contact with large numbers of cases of urinary disease is necessary for their full appreciation. In describing them I have endeavoured to give each its proper measure of importance in an estimation of the activity of the kidneys.

The physiological tests of the renal function have acquired, in the short time that has elapsed since their introduction, an important place in diagnosis. In this volume I have considered the clinical application of these methods in urinary surgery, and have given prominence to those which experience has taught me provide the most reliable information.

Some of the matter herein contained has already appeared in the pages of the *Practitioner* and of the *Clinical*

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Journal in the form of critical reviews and clinical lectures.

When the Council of the Royal College of Surgeons of England did me the honour of electing me to deliver the Hunterian Lectures for 1907, I had intended to treat this subject in detail, but the time allotted precluded anything more than a bare outline of the questions involved.

The more extended discussion of the subject presented in this volume may, I venture to hope, serve as a basis for further work. The illustrative cases are drawn from my private and hospital practice, and I gladly take this opportunity of thanking the professional friends who have entrusted their patients to my care and who have shewn interest in the diagnostic methods employed.

For such prolonged and special observations the co-operation of a competent and enthusiastic staff of house surgeons and nurses was essential, and this have I enjoyed at St. Peter's Hospital and the North-West London Hospital.

Two charts have been borrowed from Professor Albarran's work on renal exploration, and one from an article by MM. Claude and Balthazard, and one figure has been drawn from a photograph kindly sent to me by Professor Johnson Symington. With these exceptions the charts, figures, and plates are all from my own cases, and were drawn by Messrs. Shiells and Ford. To these artists, and especially to Mr. Shiells, my grateful thanks are due.

My friend Dr. Ogier Ward has helped me with the proof-sheets, and I have to acknowledge his care and valuable criticisms.

J. W. THOMSON WALKER.

30, QUEEN ANNE STREET,
LONDON, W.

CONTENTS

PAGE

INTRODUCTION 1

PART I

ESTIMATION OF THE TOTAL RENAL FUNCTION

CHAPTER I

SYMPTOMS AND SIGNS OF FAILURE OF THE RENAL FUNCTION

Cases Illustrating Different Types—Frequency and Importance of Symptoms—Local Signs—Exploration of the Kidneys 5

CHAPTER II

EXAMINATION OF THE URINE

Chemical Composition of the Urine—Variations due to Extrarenal Influences—Urea—Chlorides—Quantity of Urine—Polyuria—Oliguria—Anuria 32

CHAPTER III

THE KIDNEY AS A FILTER

Physiology of the Renal Function—Cryoscopy of the Urine—Cryoscopy of the Blood—Method of Wright and Kilner—Electrical Resistance of the Urine and Blood—Surface Tension of the Urine 52

CHAPTER IV

ELIMINATION OF CERTAIN SUBSTANCES BY THE KIDNEYS

PAGE

Historical—Evolution of Tests Based upon the Elimination of Certain Substances by the Kidneys—Methylene Blue Test—Technique of Methylene Blue Test—Condition of the Blood and Urine during the Test 83

CHAPTER V

ELIMINATION OF CERTAIN SUBSTANCES BY THE KIDNEYS (*concluded*)

The Author's Experience of the Methylene Blue Test—An Estimation of its Value—Indigo-carmine Test—Rosaniline Test—Iodide of Potassium Test—Salicylate of Soda Test—The Toxicity of the Urine . . . 104

CHAPTER VI

THE GLANDULAR FUNCTION OF THE KIDNEY

The Phloridzin Test—Technique of the Test—The Test in Renal Disease—Value of the Test 129

PART II

ESTIMATION OF THE FUNCTION OF ONE KIDNEY

CHAPTER I

METHODS OF DIAGNOSIS DEPENDING UPON CLINICAL EXAMINATION, STATISTICS, AND PATHOLOGY

Symptoms of Renal Failure—Local Signs of Disease—Absence of General and Local Symptoms—Statistics of Bilateral Renal Disease—Application of Statistics—Malformations of Genital System—Collected Cases of Anuria following Operation 146

CHAPTER II

CYSTOSCOPIC EXAMINATION OF THE URETERIC OPENINGS

PAGE

The Efflux—Absent Efflux—Copious Efflux—Murky Efflux—Purulent Efflux—Hæmorrhagic Efflux—Difficulties in Finding Ureteric Orifice—Absent or Displaced Orifice—Pathological Changes at the Orifice—Chromocystoscopy 159

CHAPTER III

METHODS OF SEPARATION OF THE URINE OF EACH KIDNEY

Evolution of Methods—Separators—Technique of Separation of Urines—Catheterisation of Ureters—Catheter Cystoscopes—Ureteral Catheters—Sterilisation and Preservation of the Instruments 176

CHAPTER IV

THEOPERATION OF CATHETERISATION OF THE URETERS

Preparation of the Bladder—Finding and Approaching the Ureteric Orifice — Introduction of Catheter — Direct Catheterisation of the Ureters by Kelly's Method—Fallacies, Difficulties, and Dangers of Catheterisation of the Ureters—Choice of an Instrument for Separation of the Urines 203

CHAPTER V

EXAMINATION OF THE URINES OF THE TWO KIDNEYS

Variation in the Activity of Healthy Kidneys—Modification of the Function by the Use of the Separator or Catheter—Variation where one Kidney is Diseased—Cryoscopy of the Urines—Chemical Examination of the Urines . . 223

CHAPTER VI

TESTS FOR THE FUNCTIONAL ACTIVITY OF EACH KIDNEY

Methylene Blue Test—Indigo-carmine Test—Phloridzin Glycosuria Test—Albarran's Experimental Polyuria Test—Practical Application of the Methods of Estimating the Functional Activity of the Kidneys 235

CHAPTER VII

FALLACIES IN THE METHODS OF ASCERTAINING THE FUNCTIONAL ACTIVITY OF THE KIDNEYS

PAGE

Greater Accuracy of Recent Methods—Partial Activity of the Kidneys in Health—Difference between Ordinary and Potential Activity—Temporary and Permanent Depression of Function—Hypertrophy . . . 257

APPENDIX: Cases of Death from Anuria and Uræmia immediately following Operations upon the Kidney . . 265

INDEX 271

ILLUSTRATIONS IN THE TEXT

FIG. PAGE

1. Patient demonstrating posterior renal pain . . . 19
2. Beckmann's apparatus for estimating the freezing point of the urine 55
3. Apparatus for measuring electrical conductivity of urine 76
4. Donnan apparatus for measuring the surface tension of urine 80
5. Apparatus used for quantitative estimation of methylene blue in urine 95
6. Irregular grey blood-clot projecting from left ureter in case of hæmaturia 164
7. Double ureteric orifice in left side 168
8. Solitary displaced kidney with two ureters, each of which opened in the natural position in the bladder . . 169
9. Chromocystoscopy 174
10. Luys' separator 182
11. Luys' separator 183
12. Cathelin's separator 186
13. Cathelin's separator in position in bladder . . . 187
14. Cathelin's separator complete, with membrane expanded, fixed on stand 188
15. Cathelin's separator in position in male subject . . 189
16. Nitze catheter cystoscope 191
17. Aseptic ureteric catheter sheath attached to modified Nitze catheter cystoscope 192
18. Casper catheter cystoscope 193
19. Albarran's catheter cystoscope 194
20. Freudenberg's catheter cystoscope complete . . 195
21. Parts of Freudenberg's catheter cystoscope . . . 195
22. Transverse section of Freudenberg's catheter cystoscope 196
23. Ureteral catheter 197
24. Author's ureteral catheter 198
25. Nitze catheter cystoscope in jar of lotion ready for use 200
26. Author's universal catheter and syringe nozzle . . 201
27. Tube for catheter, syringe, etc. 201

FIG. PAGE
28. Glass syringe for bladder washing 204
29. Catheter approaching ureteric orifice 206
30. Catheter lying in ureter 207
31. Kelly's speculum 209
32. Kelly's dilator 210
33. Kelly's ureteral searcher 211
34. Catheter at rigid ureteric orifice 214

CHARTS

CHART PAGE

1. Temperature and urine in obstructive anuria, shewing subnormal temperature and practically complete anuria, interrupted by a copious polyuria . . 8
2. Temperature chart in suppression of urine following internal urethrotomy 10
3. Temperature chart in septic pyelonephritis . . 13
4. Continuous subnormal temperature in septic pyelonephritis 26
5. Urine chart in case of enlarged prostate with polyuria 39
6. Temperature and quantity of urine in a case of chronic suppurative pyelonephritis with acute exacerbations . 41
7. Increased secretion of urine with raised specific gravity and percentage of urea after nephrectomy in case of calculous pyonephrosis 43
8. Quantity of urine in case of stricture of the urethra and pyonephrosis . . . . . *To face p.* 46
9. Chart to illustrate method of Claude and Balthazard . 64
10. Elimination of methylene blue in a healthy individual *To face p.* 88
11. Elimination of methylene blue in healthy subject prolonged to fifth day 90
12. Elimination of methylene blue in healthy subject prolonged to seventh day 91
13. Enlarged prostate, interstitial nephritis . . . 93
14. Normal elimination of methylene blue and chromogen compared with quantity of urine during first twenty-four hours after injection 96
15. Intermittent elimination of methylene blue in a case of syphilis 98
16. Intermittent elimination of methylene blue in healthy individual 99
17. Elimination of methylene blue and chromogen in a healthy individual . . . . . *To face p.* 104
18. Elimination of methylene blue in tuberculous kidney . 113
19. Pyonephrosis. Elimination of blue and chromogen after nephrectomy 117

CHART PAGE
20. Normal glycosuria after injection of 5 mgr. of phloridzin 133
21. Normal hyperglycosuria after injection of 5 mgr. phloridzin in a healthy individual 135
22. Phloridzin glycosuria in stricture of the urethra . . 138
23. Prolonged diminished phloridzin glycosuria in enlarged prostate 139
24. Normal phloridzin glycosuria after nephrectomy . . 141
25. Absence of phloridzin glycosuria in solitary diseased kidney after nephrectomy for pyonephrosis . . 142
26. Elimination of methylene blue and chromogen in a case of hydronephrosis 236
27. Phloridzin glycosuria in case of movable kidney . 243
28. Phloridzin glycosuria in calculus of left renal pelvis . 244
29. Phloridzin glycosuria in calculous pyonephrosis . . 245
30. Phloridzin glycosuria in calculous hydronephrosis . 247
31. Phloridzin glycosuria in tuberculous right kidney . . 249
32. Albarran's experimental polyuria test . . . 253

PLATES

Calculous disease of the kidney . . . *Frontispiece.*

PLATE *To face p.*

I. Chronic interstitial nephritis due to obstruction of enlarged prostate 6

II. Microscopical section of kidney in post-operative suppression of urine 11

III. Microscopical section of kidney in suppurative pyelonephritis 13

IV. Kidneys, ureters, and bladder in case of septic pyelonephritis complicating vesical, ureteral, and renal calculi 29

V. Skiagram of calculi in right kidney . . 149

VI. Fig. 1, discharge of semi-solid pus from left ureter ; Fig. 2, dragged-out ureter in tuberculous kidney 161

VII. Tuberculous kidney after nephrectomy . . 174

VIII. Calculous pyonephrosis after nephrectomy . 238

ESTIMATION OF THE RENAL FUNCTION IN URINARY SURGERY

INTRODUCTION

SINCE the pioneer nephrectomy of Simon in 1869, renal surgery has progressed step by step to nephrotomy (Annandale, 1869; Spencer Wells, and Bryant, 1870), nephrolithotomy (Morris, 1880), nephropexy (Hahn, 1881), and partial nephrectomy (Czerny, 1887).

The problem which was solved by the first nephrectomy was whether one healthy kidney could carry on the entire renal function after the shock of the operation of nephrectomy. The fear of hæmorrhage from an incision through the healthy kidney substance was the obstacle that was swept aside by Morris's nephrolithotomy, and, in addition, the proof was obtained that the wound in a healthy kidney would heal without permanent damage to the organ. In Czerny's partial nephrectomy lay additional evidence of the soundness of the latter principle.

With these fundamental principles well established, renal disease rapidly became accepted as a promising field for surgical activity. In the kidney, as in other organs, operative attack laid bare the limited means of diagnosis at the command of the surgeon, and stimulated further effort in the direction of greater accuracy. The introduction of the cystoscope,* the freer use of renal exploration as a means of diagnosis, and the application of the Röntgen rays to renal surgery,* all contributed to exact diagnosis and more successful operation.

---

* Nitze, Langenbeck's *Archiv*, Vol. xxxvi., H. 3; Leiter, "Elektro-endoscopische Instrumente," 1880.

The adoption of antiseptic methods, and the improved means of combating surgical shock, have further reduced a mortality in renal surgery which at first was unreasonably high.

But with these precautions carefully observed, there still remains a mortality in the operative surgery of renal disease against which provision has not been made. This mortality results from a failure of the renal function. The disease of the kidneys is frequently bilateral, and may be so far advanced that the renal function is only just sufficient for the wants of the individual. A failure of the renal function may be brought about in several ways.

An operation of any kind may be sufficient to overbalance the impaired renal function, and lead to suppression of urine. The frequency with which this may occur in operations which do not concern the urinary system is difficult to estimate, but it is probably not great, for the presence of advanced renal disease would be looked upon as a sufficient contra-indication to any but operations of urgency.

When the operation concerns some part of the urinary tract, however, this mortality at once becomes a prominent factor, and a consideration of the adequacy or the reverse of the renal function is likely to arise. Thus, in operations upon the lower urinary tract, suppression of urine takes a high place in the mortality figures.

Finally, in operations upon the kidney the question as to the renal efficiency becomes a matter of importance.

In the course of the following pages I shall discuss the question of the second kidney in nephrectomy, and it need only be remarked here that such a catastrophe as the removal of a kidney when the second kidney

* J. MacIntyre, *Lancet*, July 11, 1896.

is destroyed by disease, or when only one kidney has developed, demonstrates the urgent need for a complete estimation of the renal function.

But apart from the removal of the kidney, there are cases of bilateral disease in which a conservative operation upon one organ is sufficient to upset the balance of renal secretion and cause fatal suppression of urine.

It will at once be admitted that many brilliantly successful results have been obtained by operation upon cases of bilateral renal disease where the outlook seemed hopeless, and if the surgeon is to be deterred from operation in all such cases by evidence of an impaired renal function, such a method of examination "is calculated to impede the development of the surgery of the kidney." But an attempt to estimate the renal function in these cases has for its object not only the demonstration of a lowered renal function, for that may be already obvious, but the decision, if this be possible, of the question whether the function is lowered to such a degree that operation will almost certainly prove fatal.

I shall consider the subject of the estimation of the renal function, so far as it concerns surgery, under two main divisions, as follows :—

I.—The estimation of the total renal function.

II.—The estimation of the function of one kidney.

PART I

ESTIMATION OF THE TOTAL RENAL FUNCTION

CHAPTER I

SYMPTOMS AND SIGNS OF FAILURE OF THE RENAL FUNCTION

Cases illustrating different types of renal failure—Frequency and importance of symptoms—Local signs—Exploration of the kidneys

UNTIL a comparatively recent date, the surgeon has been content to rely upon the symptoms and local signs of renal disease, and the examination of the urine in order to judge of the activity or the reverse of the renal function. Before passing to the consideration of certain more recently introduced methods which may be employed to estimate the functional activity of the kidneys, it will be convenient in this and the following chapter to glance briefly at those other means by which a judgment may be formed.

GENERAL SYMPTOMS AND SIGNS

Before considering in detail the symptoms of reduced functional power of the kidneys in surgical diseases of the urinary organs, I shall relate several cases which are illustrative of types of renal failure met with in practice.

Case 1.—*Enlarged prostate; moderate bilateral hydronephrosis; chronic interstitial nephritis; operation; death from suppression of urine.*

C. S., a labourer, aged 52 years, came under my care at St. Peter's Hospital, complaining of inability to pass water and weakness of the legs. He had suffered from difficult micturition for seven years. There had been blood in his urine about once a month for the same time. For twelve months before I saw him his bladder had been distended, and the urine dribbled away. He had lost weight during six months, and suffered from headaches and occasional nausea.

He was a dull, apathetic man, with a sallow, muddy complexion. His skin was dry and harsh, and he seldom perspired. The bladder was fully distended, the prostate enlarged, smooth, elastic, and movable. The kidneys were not tender or palpable, and there was no renal pain or aching. The heart and lungs were healthy, the pulse low-tension and regular. He had a clean, moist tongue, and did not complain of thirst. His appetite was poor. The temperature was subnormal. He was put on catheter life. The urine had a specific gravity of 1010, was pale, and showed a faint cloud of albumin. The urea varied between .6 per cent. and 1 per cent. There was continuous polyuria, which frequently amounted to 80 ounces in twenty-four hours and reached 108 ounces on one occasion. There was peripheral neuritis of the legs, and some wasting.

I performed an easy and rapid prostatectomy, after which the patient rallied satisfactorily.

On the day following the operation the patient became drowsy and apathetic, and vomiting set in. The urine diminished from the third day, and complete suppression and death occurred on the fifth day. The patient was mildly delirious during the last twenty-four hours. The tongue was dry and brown.

Post-mortem, the kidneys shewed moderate hydronephrosis, the calyces and pelves of the kidneys being distended. The renal parenchyma was a dull brown colour and of rather tough consistence. Under the microscope (Plate I.) there was advanced interstitial nephritis. The

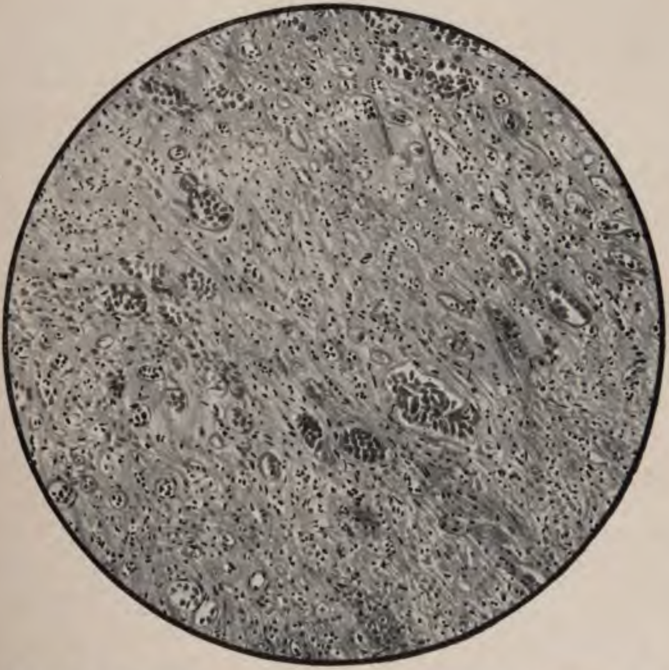

PLATE I.—Chronic interstitial nephritis due to obstruction of enlarged prostate.

bladder was healthy, and there were no signs of recent pyelitis.

Case 2.—Carcinoma of the bladder; obstructive anuria.

(This case was under the care of my colleague, Mr. Pardoe, and came under my observation in his absence. He kindly accorded me permission to watch the progress of the disease.)

F. M., a labourer, aged 42, had complained of urinary trouble for five months, but continued at work until December 5th, 1906, when he was admitted to St. Peter's Hospital with supposed retention of urine.

His symptoms had started with the passage of blood after lifting a heavy weight, and from that time he had suffered from increased frequency of micturition and intermittent hæmaturia, which appeared about twice weekly. For three days before admission he had passed a small quantity of urine. During the past week there had been some bilateral renal pain. He had lost flesh for five months. The stream of urine was good, but often stopped suddenly and recommenced after a time. The tongue was moist and slightly furred.

There was no enlargement or tenderness of the kidneys, and no thickening of the bladder base. On the day following admission he only passed two ounces of urine. I was asked to see him with a view to emptying his bladder, which was supposed to be full of clot and urine. I found the patient comfortable and without pain. His complexion was rather muddy and his skin dry. There was no headache, thirst, or vomiting. The tongue was moist and slightly furred. The bladder was not distended. There was no enlargement or tenderness of the kidneys. The temperature was subnormal. The two ounces of urine that he had passed had a specific gravity of 1020, an alkaline reaction, and contained a large quantity of albumin and some blood. The urea amounted to .6 per cent. There was no pus. A copious perspiration was induced by pilocarpin ($\frac{1}{8}$ grain). On the three following days (December 6th, 7th, and 8th) he passed two, one, and three ounces of urine respectively (Chart 1).

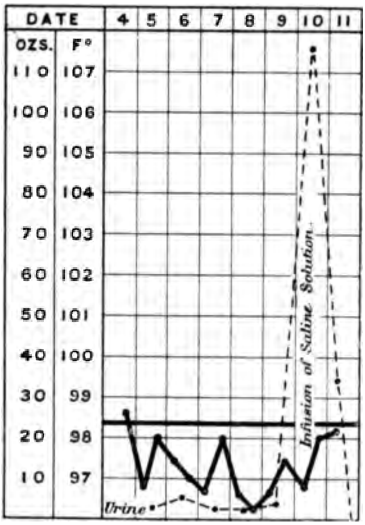

Chart 1.—Temperature and urine in obstructive anuria, shewing subnormal temperature and practically complete anuria, interrupted by a copious polyuria.

On December 8th the skin was dry and harsh, the tongue slightly moist, but the lips dry. There was a tendency to drowsiness. His breathing was forced, and occasionally assumed the Cheyne-Stokes type. The pulse was 60 per minute, low-tension and rather irregular. The pupils were medium in size and reacted well. The knee jerks were slow. There was no mental change. There was an occasional hiccough, and he began to vomit after his medicine. On December 10th he was drowsy, his face was dusky and pinched, and he lay with open mouth and half-closed lids. He was easily roused and talked intelligently, but quickly relapsed into partial unconsciousness. The breathing was jerky and forced, and at times of the Cheyne-Stokes variety. The voice was feeble and thick. The pupils were medium size, and reacted sluggishly, the tongue dry and brown, and the pulse slow (40 to 50 per minute), feeble, irregular, and intermittent, and of low-tension.

He complained that he could not move his legs. The knee jerks were abolished. He had some twitching movements of the right hand and arm. The freezing point of the blood was - 0.3° C., and of the urine - 0.71° C. An injection of phloridzin did not produce glycosuria in the scanty urine that he passed.

An infusion of two pints of saline solution into the median basilic vein revived him. Soon after he had pain in the lower part of the abdomen, which continued for some hours, and about six hours later he began to pass a very large quantity of pale limpid urine, much of which was lost, but 146 ounces were collected in twenty-four hours. This urine was clear, pale, and had a specific gravity of 1009, a freezing point of - 0.55° C., and contained 0.167 per cent. of chlorides.

On the following morning (December 10th) the mental symptoms had completely passed off. The patient was bright and cheerful, and sensible in conversation. His breathing was natural and his pulse 60 per minute, regular, and of good tension. He took food well, and was no longer sick. There was an occasional hiccough. The polyuria suddenly ceased at midnight, and after that there was only an ounce of blood-stained urine. He seemed dazed and became increasingly drowsy, and commenced to hiccough as before. This continued throughout the day (December 11th), and at 6.30 p.m. there was a sudden attack of severe dyspnœa, and he died an hour later.

Post-mortem, there was extensive carcinoma of the bladder involving both ureters, slight distension of the kidneys and renal pelvis, and a moderate degree of interstitial nephritis.

Case 3.—*Stricture of the urethra ; internal urethrotomy ; suppression of urine.*

On October 29th, 1903, I was called to see G. T., a man of 40 years, at St. Peter's Hospital, and obtained the following history. The patient had suffered from difficulty in micturition for nine years, and during the first two years had passed a No. 8 catheter himself. For six years no instrument had been passed. For three weeks previous to his admission, the urine had dribbled from an over-distended bladder. The urine had a specific gravity of 1016, was acid, and contained no pus or blood. There was no lumbar pain.

On October 28th internal urethrotomy had been performed under ether by a colleague, and a No. 16 steel instrument passed readily. The bladder was washed out and the catheter withdrawn.

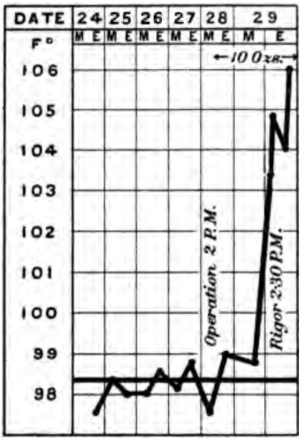

Chart 2.—Temperature chart in suppression of urine following internal urethrotomy. A microscopical section of the kidney in this case is shewn in Plate II.

On the following morning he was comfortable and had not been sick, but he had only passed two ounces of blood-stained urine, and the bladder was not distended. At 2.30 p.m., twenty-four hours after the operation, he had a rigor, and the temperature rose to 103° F., and a little later to 104.8° F. (Chart 2). At 3.45 the patient became very restless, trying to get out of bed and constantly muttering. The pulse was very small and fast—130 per minute. Five ounces of bloody fluid were withdrawn from the bladder, but it was doubtful if this was urine or fluid left in the bladder at the time of operation.

At 7 p.m. he was drowsy, his pulse was imperceptible, and temperature 104° F. The pupillary reflex was slow. At 10 p.m. the temperature was 106° in the rectum, the lips and ears were dusky, the nose cold, and the skin sweating slightly. The breathing was rapid and faintly stertorous, he was unconscious, tossing about and moaning at intervals. I saw him at this time, and hoped that by

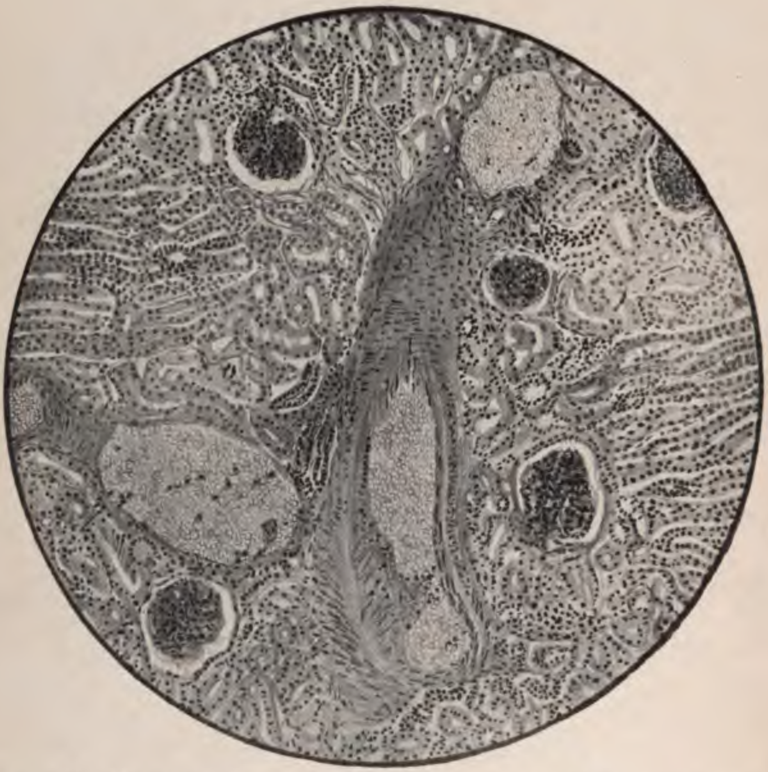

PLATE II.—Microscopical section of kidney in post-operative suppression of urine. Engorgement of blood-vessels. Nuclei of renal epithelium well stained.

relieving the renal tension the function of the kidneys might be restored.

I rapidly exposed the right kidney. The fatty capsule was thick and coarse, the true capsule white and opaque. The kidney was flabby, and its consistence did not differ from the normal. The capsule was rapidly stripped off the kidney. The substance of the organ was dark and congested, but not otherwise changed. The whole operation did not last more than ten minutes, and caused no change in the condition of the patient. A pint of saline solution was introduced into the rectum, and two pints infused into the median basilic vein, and the pulse improved somewhat, but remained about 140 per minute.

At 11.30 p.m., 33 hours after the urethrotomy and 9 hours after the preliminary rigor, the patient vomited some brown material, and died. The right kidney was removed two hours later. It was plum coloured and flabby. There was no appearance of distension or interstitial nephritis. At the base of the pyramids the vessels seemed engorged with blood, the cortex was dark in colour, and the pyramids paler. The structure was clearly defined. A microscopical section shewed the veins at the base of the pyramids distended with blood, and in the cortex also some of the vessels were engorged. A few of the pyramids and one or two of the glomeruli shewed dilated vessels. The glomeruli and tubules appeared healthy, and the nuclei of their cells well stained (Plate II.).

Case 4.—*Acute suppurative pyelonephritis following the introduction of a catheter in prostatic obstruction; cystotomy and nephrotomy; recovery.*

J. F., a barman, aged 60 years, was sent to me at St. Peter's Hospital by Dr. H. E. Strickland. For four months he had experienced difficulty in micturition. He waited three or four minutes before the urine began to flow, and strained during the act. The stream was small and dropping, and there was dribbling at the end of micturition. During the day he passed water about 10 or 12 times, and at night he wore an apparatus. There was dull, heavy suprapubic pain and bilateral posterior renal aching. He suffered from headache, constant burning thirst, and loss of appetite, but there was no emaciation. The tongue was moist and furred. The bladder was distended to the umbilicus, and the prostate enlarged. There was bilateral renal tenderness, and his skin was dry. He was admitted to hospital, and his urine slowly drawn by a fine catheter, which was tied in place. In 24 hours 84 ounces of urine were passed, with a specific gravity of 1016 and containing 1.1 per cent. of urea. After five days the catheter was removed, and then for two days the urine was withdrawn by catheter by the house surgeon. On the second day there was a rigor, and the temperature rose from normal to 101.6. There was burning thirst, headache, and increased tenderness over the kidneys. On the following day there was a second rigor, and tenderness over the kidneys became marked, and the abdominal muscles were rigid on both sides. On the third day hiccough commenced, and on the next day became severe. I was asked to see him on the fifth day following the infection. At this time his face was dusky, pinched, and drawn, and his eyes sunken. His tongue was tremulous and coated with a white fur, but not dry. He suffered from intense thirst, and his skin was dry. The hiccough had now become distressing. There were five spasmodic jerks of the diaphragm following rapidly upon each other, so that a peculiar inspiratory wail was produced and recurred after a pause of only five seconds. The urine was alkaline and foul, and contained an abundant deposit of pus. There was now no marked rigidity of the abdominal wall, and the left kidney was no longer tender. The right kidney was enlarged and tender. The amount of urine in 24 hours was four ounces. On the following day the face

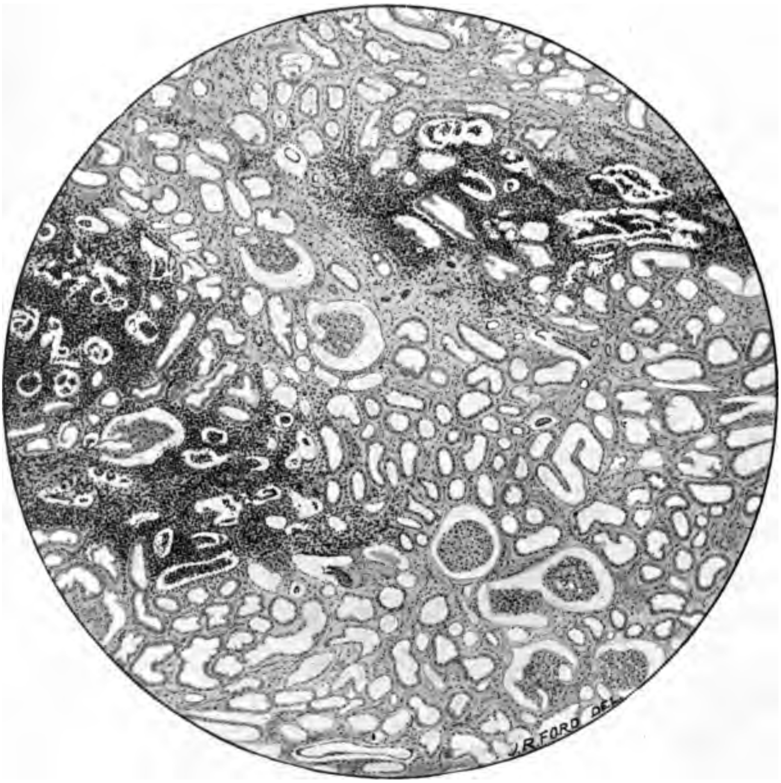

PLATE III.—Microscopical section of kidney in suppurative pyelonephritis. The field shews the edge of the affected area and illustrates the spread of inflammation along the line of the tubules.

was dusky, the lips blue. The patient was unconscious at times, with upturned eyeballs and half-open lids.

I decided to operate, and rapidly opened and drained the bladder and then exposed the right kidney. The kidney was large and toughly adherent to the diaphragm and liver. The surface shewed the yellow mottling of suppurative pyelonephritis. I incised the curved border very freely, laying the organ open for about 2½ inches and cutting into the pelvis. A large drainage tube was introduced into the pelvis, and the kidney wound closed round this. A slip of kidney tissue was removed, and on microscopical section shewed the typical appearance of ascending suppurative pyelonephritis, streaks of round-cell infiltration passing outwards through the medulla to densely infiltrated masses in the cortex, which were beginning to break down at some spots (Plate III.).

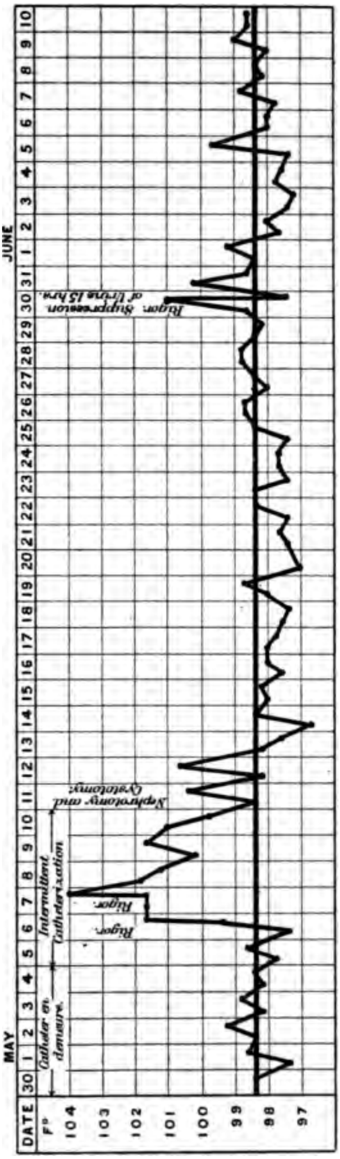

Chart 3.—Temperature chart in septic pyelonephritis. Case of enlarged prostate. Infection conveyed by catheter. Recovery after nephrotomy and cystotomy. Subsequent suppression of urine following exploration of cystotomy wound.

On recovery from the operation two pints of saline solution were infused into the median basilic vein. The renal function was re-established in a few hours. On the following day the patient's mind was again perfectly clear, and his temperature falling. The hiccough had practically ceased. In 48 hours after the operation the drawn, anxious look had left his face and the dusky hue had gone.

He continued to improve for 18 days after the operation. On the morning of the 19th day the suprapubic wound was explored by the house surgeon with the finger. Half an hour later the patient had a rigor, and the temperature rose to 100.8° (Chart 3). Some hæmorrhage took place from the wound in the kidney, and it was found that the secretion of urine had ceased. The face assumed an anxious, drawn look, and had already become a little dusky. The pulse was 100, feeble and irregular, the skin dry, and the tongue glazed. The suppression continued for 15½ hours. After intravenous infusion of saline solution the renal function was again resumed. After this, convalescence was uninterrupted.

The after-history of this case was as follows. Three and a half months after the nephrotomy for pyelonephritis the kidneys were secreting well and a hard enlarged prostate was removed by the perineal route. Microscopical sections shewed that the tissue was malignant in nature. The patient made an uninterrupted recovery from the operation.

Case 5.—*Malignant enlargement of the prostate, urinary septicæmia, prostatectomy ; death three months later from renal failure.*

General C., aged 81, was referred to me by Dr. Robert Fergusson, suffering from enlarged prostate and urinary septicæmia. The patient had been passing a catheter to draw off his water for several years. He had previously had several attacks similar to that in which I first saw him, but not so severe. I saw him on April 23rd, 1906, with Dr. Fergusson. There had been difficulty in passing the catheter. The temperature was 102°, and his mind was wandering at times, although he could be recalled by a sharp question. He was in a low, feeble condition. His face was rather dusky and his lips blue. The tongue was dry and glazed. He suffered from constant thirst, but refused all solid food. The prostate was large, bilobed, movable, elastic, and regular. The bladder was partly distended with foul, stinking urine. There was prolapse of the rectum.

The attack passed off under treatment, but the urine remained foul, and he was becoming less able to attend to the details of catheterisation and bladder washing. His tongue was moist and furred, and his appetite fair. The pulse was good, although his arteries were rigid. There was no bronchitis.

I decided to operate, and on June 7th performed prostatectomy. The prostate projected as a cone into the bladder, and the earlier part of the enucleation was easy. At the rectal surface of the prostate, however, the gland was firmly adherent to the sheath, and was separated with difficulty, leaving a tough leathery wall to this part of the prostatic cavity.

The patient rallied well after the operation. On the following day the tongue was moist, the temperature normal, and the kidneys acting well, although his urine continued to be foul. The wound healed slowly after some sloughing of the edges, and finally closed on July 3rd, four weeks after the operation. The patient's general condition gradually improved. His tongue was moist but furred, his appetite good, and he steadily gained ground and returned home six weeks after his operation with the bladder wound closed. His urine was still foul and frequent washing of his bladder was necessary, but his general condition was good. Nine weeks after the operation he began to lose ground. The doctor in charge found more and more difficulty in washing the bladder, and the urine became increasingly foul. The suprapubic wound broke down again. He began to lose flesh, and rapidly became emaciated. The skin was dry and scaly. The tongue was dry and glazed, and the throat parched. He was thirsty and took fluids, but absolutely refused all solid food. The temperature was sometimes a little raised, usually it was subnormal. The pulse continued strong, but was intermittent and at times irregular. He wandered a little at night, but during the day retained his faculties. There was no headache, no renal pain or tenderness, and no enlargement of the kidneys. The urine was foul, and contained pus and a little blood and *débris*. The quantity became reduced to about 10 or 15 ounces a day, but it could not be accurately measured, as the suprapubic wound had opened again. For several days he refused all nourishment and rapidly failed, and he died three months after the operation.

Case 6.—Bilateral renal calculus; failing renal function; anuria; death.

R. S., a publican, aged 46, came under my care at St. Peter's Hospital. For six years he had suffered from bilateral renal pain. The pain in the right kidney had subsided, but the left continued to ache. Five years ago he passed several small rough stones, and had passed some since, the last two years ago. The pain in the left kidney was sharp, and came on in attacks which walking seemed to precipitate. During an attack there was also pain along the left ureter, shooting into the left testicle. There had only once been hæmaturia during an attack of pain. The attacks occurred about once a month, and were accompanied by vomiting and retching. There had been pain in the hollow of the right foot during an attack, and he complained at times of numbness of the thighs. He had recently lost flesh, and had suffered from severe thirst for 2½ years. He was a thin, poorly-nourished man, with a sallow complexion. His skin was dry, and he seldom perspired. There was no œdema of the legs or feet. There was no headache, but he complained of constant thirst. There was tenderness over the right kidney, and a hard nodular mass could be felt. The left kidney was not tender or palpable. He was passing a large quantity of murky, alkaline urine hourly during the day and night. The bladder showed chronic cystitis. The left ureteric opening was large, round, open, and the edges rigid looking, the right small and closed. Both were pumping slightly murky urine. The urine was alkaline or neutral, and gave a considerable deposit of pus on standing. The specific gravity was 1014 and the urea amounted to only .8 per cent. The X-rays shewed large masses of calculi in both kidneys. I did not consider him suitable for operation. He attended at the hospital for 18 months without much change taking place, and then I was called to see him by Dr. J. W. B. Steggall. He had been feeling ill for about 14 days, and was drowsy and slept much. He was sick and constipated. The quantity of urine secreted was small. When I saw him he was drowsy, and took little notice of his surroundings, but could be roused. His pupils were moderately contracted and reacted to light. His face was sallow, his tongue becoming dry. The pulse was feeble and irregular. He took no nourishment. No urine had been passed for 12 hours, and there was none in the bladder. He sank and died some hours later.

The foregoing cases illustrate different types of urinary disease in which the factor of chief importance was the functional power of the kidneys. These cases have been selected because the symptoms were pronounced, and the diseases far advanced. There are, however, many cases of surgical disease of the kidneys, whether primary in these organs or secondary to disease of the lower urinary tract, where the symptoms of renal failure are less pronounced or even insignificant. It is necessary, therefore, to turn to cases where renal disease is less advanced, and to consider what symptoms of renal failure are displayed by such patients.

I examined 109 cases of simple enlargement of the prostate with a view to ascertaining whether symptoms of renal failure were present. In all these cases the obstruction was sufficient to interfere with the complete emptying of the bladder. The amount of residual urine varied from a few ounces to complete retention. Some of the patients were unaware of the residuum; others had their bladder greatly distended, and the urine dribbled away in passive overflow. Others, again, passed a catheter occasionally, and some were absolutely dependent upon this means of voiding the urine. Thus the amount of obstruction, if measured by the condition of the bladder, varied, and the pressure against which the urine was secreted might be expected to vary in similar measure. The symptoms of renal inadequacy did not, however, always follow the variations in the mechanical defect in the bladder. They might be well marked with an ounce or two of residual urine, and poorly developed or quite absent when the bladder was fully distended. Thus no symptoms of renal inadequacy were present in 25 of these cases (22.9 per cent.), and the bladder was fully distended in three of these and the patient dependent upon the catheter for relief in four.

Again, in 100 cases of stricture of the urethra attending my out-patient department at St. Peter's Hospital,* 65 had no symptoms of renal inadequacy, and 35 had more or less marked signs. Some of those with symptoms of impaired renal function were narrow strictures, admitting only about a No. 6 French bougie (9 cases). But, on the other hand, symptoms were marked in some patients with stricture admitting large steel bougies (13–15 and 14–16).

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* I am indebted to my late clinical assistant, Dr. J. O. Glass, of Cleveland, Ohio, for much patient work in collecting the details of these cases during a period of six weeks.

As a rule, in those cases of large calibre strictures, where symptoms of renal inadequacy were present, sepsis had been superadded, and the urine was cloudy or even foul (11 cases). In some cases (3) there was the combination of a very narrow stricture with septic urine. In 12 cases with renal symptoms the stricture was of large calibre and the urine aseptic, but in these cases the strictures had existed for long periods of time, and had at one time been very narrow, and some of them had been cut with the urethrotome.

I shall now consider each symptom and sign of disease of the kidneys separately, leaving the examination of the urine for a subsequent chapter.

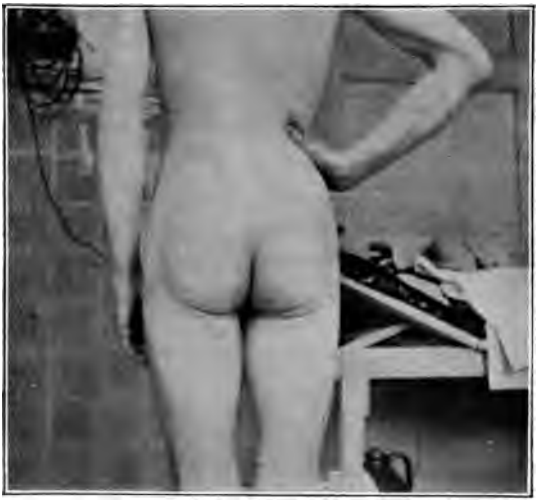

Fig. 1.—Patient demonstrating posterior renal pain.

Pain.—Pain was one of the most frequent signs of renal disease in these cases. There was pain referred to the kidneys in 31 of 109 cases of enlarged prostate, in 22 out of 100 cases of stricture, and in 53 in 209 (25.3 per cent.) cases of urinary obstruction.

The pain was situated, in the greatest number of these cases, at the angle formed by the erector spinæ mass of muscles with the last rib, and was usually localised by the patient tucking his thumb into this spot * (Fig. 1).

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* Author, "A Clinical Lecture on Pain as a Symptom in Urinary Disease," *Clinical Journal*, Feb. 8, 1905.

Occasionally it was diffusely spread across the loins in this region. It was bilateral in all the cases (31) of enlarged prostate. In the stricture cases it was bilateral in 10, and unilateral in 12 (6 right and 6 left).

The pain had usually a constant, dull, aching character. In a few of the cases of stricture the pain was only present during micturition. In one patient, who volunteered this information, the pain gradually diminished during intermittent dilatation of his stricture, and finally disappeared completely. I looked upon this type of pain as an indication that the sphincter action of the lower end of the ureter had been destroyed by the back pressure of the urine. In only one case, of enlarged prostate, was there any tenderness of the kidneys.

Thirst.—The most frequent symptom of interference with the renal function was thirst. 35 out of 109 patients suffering from enlarged prostate complained of this symptom, and it was present in 21 out of 100 cases of stricture. Thus there were 56 in 209 (26.7 per cent.) patients with urinary obstruction in whom this was the subject of complaint. Several of these remarked an increased severity of the symptom during the night hours. The thirst was often present without any dryness of the tongue or mouth (26 in 35).

Tongue.—A dry tongue is an important index of the state of the renal function. In cases of urinary disease under continuous observation over prolonged periods it will be found that the tongue varies according to the fluctuations in the renal function. The tongue is first dry along the centre and rather red, later it becomes dry over its surface, and has a glazed and often cracked appearance. A dry tongue, covered with a brownish fur (parrot tongue), is present in the later stages of urinary septicæmia. There was a dry tongue in 10 cases of prostatic obstruction and 17 cases of stricture (12.9 per cent.).

Anorexia, dysphagia, nausea, vomiting.—With a dry tongue and thirst there is often a loss of appetite. This was the subject of complaint in 5 per cent. of these cases of urinary obstruction, but it was present in a minor degree in a much larger number of cases. In the more severe grades of renal destruction this disinclination for food becomes a prominent feature of the case. With the dry tongue and parched throat it becomes more and more difficult to swallow solid food, and a " buccal dysphagia " becomes established. Fluids are usually eagerly taken, but in the later stages even this form of nourishment may be refused. Nausea is often present, but vomiting only occurs as a complication of the latest stage of the disease. At first it only occurs after taking medicine or food, but later without such stimulus. It is accompanied by retching and straining. Constipation is frequently present, and is a well-known complication of prostatic disease.

Headache.—Headache is a feature of many of these cases. It is present in the morning on rising, or may be troublesome all day. It is usually frontal, sometimes at the vertex, and rarely occipital. It was the subject of complaint in 22 per cent. of these cases of urinary obstruction. Giddiness and slight losses of memory accompanied this symptom in a few cases.

Skin.—In the later stages of " urinary septicæmia " the face has a peculiar yellow, earthy look that is almost characteristic. In less advanced cases there is often a sallow, muddy complexion that points to chronic toxæmia.

The skin is often dry and harsh, and these patients seldom sweat. In cases where exacerbations of septic pyelonephritis occur from time to time, the fall of the temperature may, however, be accompanied by profuse sweating.

Emaciation.—There was appreciable loss of weight in 19 per cent. of these cases. Emaciation is often present to a slight degree in cases of aseptic renal destruction, but it is most striking where sepsis is superadded. The patient suffering from septic pyelonephritis seems to shrink within a few hours of the rise of temperature which ushers in the inflammation. The eyes are sunken, the cheeks and temporal fossæ hollow. There is a progressive and rapid loss of flesh. The patient is reduced in a few weeks, or even in a shorter time, to an extreme degree of emaciation. So rapid and extreme may the loss of flesh be that the question may arise as to the presence of some malignant growth.

In my own cases the most rapid and extreme emaciation was observed in patients who had suffered from long-standing vesical calculus with ascending pyelonephritis. In less advanced cases loss of flesh is still a significant symptom, although present to a less degree. In such cases recurrent exacerbations of renal inflammation are accompanied by a rapid loss of flesh, and when the attack is over the weight again rises to its previous figure.

Hiccough.—Associated especially with septic renal changes, hiccough is a sign of grave import. Its incidence after an operation upon the lower urinary tract may be looked upon as a signal for alarm. At first the spasms occur at long intervals, and may be soothed by a draught of fluid ; gradually they become more frequent, until they recur at short intervals and exhaust the patient's strength. The most severe form of hiccough that I have observed was in the case already related (Case 4, p. 11), where the spasms ran in closely following series of five, which eventually merged into a peculiar crowing inspiration. The spasms ceased under an anæsthetic. This patient recovered after nephrotomy, slight hiccoughs occurring at lengthening intervals during the two days following the operation.

Mental and nervous phenomena.—In the chronic cases of aseptic or septic pyelonephritis, there is nothing to warn the surgeon of the delirium that may sometimes follow surgical interference, even of a minor degree. The passage of a sound or cystoscope under an anæsthetic is sometimes followed in these cases by a critical period of restless delirium. In the later stages of the disease, in the crisis that may follow an operation for the relief of the obstruction, and in the gradual failure of the renal function when operative interference has been too late, drowsiness is a prominent symptom. The patient sleeps heavily and continuously, he is wakened for nourishment, and at once relapses into slumber. This may pass off after the first few days following an operation, but it is always a grave symptom. This drowsiness may be replaced by or alternate with a mild muttering delirium; often it passes into coma and death.

In cases of fatal post-operative suppression of urine, there is frequently a period of restless delirium, rapidly followed by coma. This stands out in strong contrast with the mental state in the condition known as obstructive anuria. Here the mind remains clear and unclouded for days, although the renal function is completely suspended.

There are seldom any of the nervous phenomena that are observed in Bright's disease. Some twitching of the fingers, which may extend to the muscles of the arms and legs, may be noted. The patient may also complain of inability to move his legs, and may lose sensation in them, but there is no actual paralysis.

The knee-jerks become sluggish, and may for a time be abolished. The pupils are rather small, and are sometimes contracted. They react sluggishly to light. Convulsions, if they occur at all, are extremely rare. Uræmic dyspnœa is observed in some of the advanced cases. It may be slightly marked for some days in a case of anuria, and then become paroxysmal. Cheyne-Stokes breathing is not unfrequently observed in the last stages.

Temperature.—I have not been able to satisfy myself that in cases of interstitial nephritis from urinary obstruction a rise of temperature is to be found apart from septic complications.

The point is a difficult one to settle, the more so that in some cases of undoubted septic infection of kidneys, previously the seat of interstitial nephritis, the gross *post-mortem* appearances of the kidneys do not differ very greatly from those of aseptic interstitial nephritis. Mr. Henry Morris* has drawn attention to this latter point, and my experience is in agreement with his observation.

In cases where the kidney is being slowly destroyed by increased urinary pressure caused by obstruction (stricture, enlarged prostate, etc.), the temperature is slightly subnormal when sepsis is not present (aseptic pyelonephritis).

Where the obstruction is absolute (calculous obstruction, blocking of the ureters by malignant growths of the bladder, uterus, etc.), the temperature is continuously subnormal (Chart 1, p. 8).

The renal efficiency in these two groups of cases might appear at first sight to differ widely, for the secretion of large quantities of urine is a characteristic feature of advanced aseptic pyelonephritis, while with more complete obstruction there is anuria. But the difference is not great, for the copious polyuria of aseptic pyelonephritis is the state of renal failure which is nearest to complete suppression.

Septic pyelonephritis may be engrafted upon aseptic pyelonephritis, or it may be induced when the kidneys are practically healthy. The onset of septic pyelonephritis is heralded by a rigor which is usually pronounced, and the temperature shoots up to 103 or 104, or even to 105° F. With this the quantity of urine secreted is greatly reduced, the patient is drowsy and indifferent to his surroundings, his tongue is dry and often furred, but sometimes glazed and cracked, there is renal aching and tenderness, and either a flat abdomen, somewhat rigid on one side, or a distended, tympanitic belly.

The further progress depends to some extent upon the severity of the infection and the resistance of the patient.

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* "Surgical Diseases of the Kidney and Ureter," Vol. i., p. 307, 1901.

The rigor may be repeated, and the temperature, after a slight drop, rises to the same height or higher. If the toxæmia continues, and if there is unrelieved obstruction in the lower urinary tract (enlarged prostate, narrow stricture) it is likely that it will do so, the temperature remains high and swinging, the patient becomes increasingly drowsy, hiccough and vomiting set in, and death takes place at the end of five or six days, often after a fall of the temperature. On the other hand, the temperature may fall gradually during two or three days, or rapidly during 24 hours, to normal, and the preliminary attack is over. There are many cases in which no further trouble ensues; the urinary obstruction, which was the keynote to treatment, has been relieved. With the drainage or re-establishment of the natural outflow, the absorption of toxic material has ceased, and the pyelonephritis has subsided. But there are also cases in which the course is not so fortunate. Because of the continued obstruction, or sometimes in spite of its relief, the patient has from time to time periodic rises of temperature, sometimes excited by incautious exposure or surgical interference, but often without ascertainable cause, and ushered in by a slight chill or even a fully developed rigor. These attacks may recur at fairly regular intervals of 10 or 14 days. They resemble the preliminary attack, but are often less violent in their course. Between these attacks the temperature is usually subnormal; often it may be so for long periods of time (Chart 4, p. 26), but the patient is losing ground, he is becoming rapidly emaciated and feeble. Finally, one of these attacks carries him off, or he may die asthenic and emaciated by a gradual process of exhaustion.

The surgeon may meet with the case in the interval of subnormal temperature, and there may be little in the symptoms to shew how advanced is the disease of the kidneys. An acute exacerbation may be caused by the incautious passage of a catheter or bougie, or the patient may gradually sink without apparent cause, and die of exhaustion some weeks after an operation.

The accompanying chart (Chart 4) shews a continuous subnormal temperature in a case of chronic septic pyelonephritis (case H. T., p. 28).

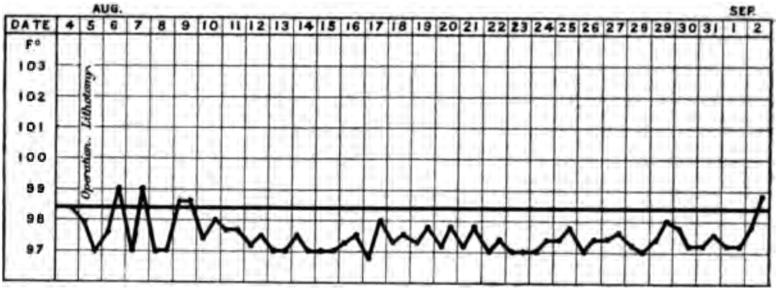

Chart 4.—Continuous subnormal temperature in septic pyelonephritis. The kidneys, ureters and bladder of this case are illustrated in Plate IV.

In post-operative suppression of urine there is a rigor a few hours, or as long as 24 hours, after the operation, and the temperature shoots up to 103° or 104° F. and remains high, sometimes reaching 105° or 106° F. The course is usually rapid. After a period of restless delirium, the patient becomes comatose, and sometimes dies within 12 hours of the rigor (Chart 2, p. 10).

Circulatory changes.—Œdema is usually entirely absent in these cases. In some advanced aseptic and in a few septic cases, I have noted a faint œdema of the abdominal wall, but there is never œdema of the legs and other parts, such as may be observed in Bright's disease; nor are the cardio-vascular changes, so characteristic of chronic Bright's disease, present in these surgical cases. The pulse is usually soft and sometimes irregular, and the arterial wall may be calcareous, but it is not sclerosed.

In advanced aseptic pyelonephritis, and especially where anuria is present, the pulse is slow (from 60 to 75 per minute), its tension low, and the beat irregular and often intermittent. In acute septic pyelonephritis the pulse shews the effect of the fever, being full in volume and rapid. In the cases of fatal post-operative suppression it quickly becomes running and uncountable.

In chronic cases of urinary septicæmia the pulse shews little change. It may be irregular and intermittent.

LOCAL SIGNS

I have already referred to renal pain as a symptom in cases of urinary obstruction.

Tenderness.—In examining the kidneys by palpation they may sometimes be found tender on one or both sides. This sign is, however, rare, and is present only in cases where septic inflammation is a feature. In septic pyelonephritis the tenderness is usually, after the first day or two at least, confined to, or most marked on, one side.

Frequently, however, the kidneys may be far advanced in septic pyelonephritis without any tenderness being observed after repeated palpation.

Rigidity.—It is not unusual to find some degree of rigidity of the abdominal muscles on one side, but this is subject to considerable variation, and it appears to be most marked during the earlier part of an acute attack of pyelonephritis.

Enlargement.—The hydronephrosis which results from urethral obstruction is never sufficiently large to admit of its recognition by palpation ; nor is the kidney palpable in chronic septic pyelonephritis, which so frequently complicates long-standing cases of vesical calculus or enlarged prostate. But in the more acute cases of septic pyelonephritis of recent origin it not infrequently happens that a large, tender kidney can be felt on one side. In pyonephrosis, which may complicate obstruction in the lower urinary tract, the enlarged kidney can usually be felt. It may, however, be obscured by muscular rigidity of the abdominal wall, and even a large pyonephrotic kidney may thus be concealed.

In the foregoing pages the symptoms of renal disease complicating disease of the lower urinary tract have been discussed.

It may happen, however—and the experience cannot be counted rare—that in dealing with some disease of the lower urinary tract all the ordinary means of investigation are used without revealing any sign of disease of the kidneys, yet the progress or after-history of the case shews that advanced disease of these organs has been present. This is most likely to occur where the surgeon is dealing with tuberculous and calculous diseases of the bladder.

The following case of calculous disease may be quoted in illustration :—

H. T. (II. 372 W.), a French polisher, aged 37, came under my observation at St. Peter's Hospital in August, 1904. He complained of frequent micturition, and gave a history of eight years' intermittent treatment of stricture of the urethra. For 15 months he had suffered from pain at the end of the penis after micturition, and this had been worse during the past three months, when the urine has been turbid and foul. During three months there had been occasional hæmaturia. He passed urine every half-hour to one hour during the day, and it dribbled from him at night. The stream often stopped suddenly during micturition, and there would then be severe perineal and penile pain. There had been no renal pain or colic. He was a fairly nourished man. The tongue was moist and clean, and the appetite good. The urine was alkaline and foul, specific gravity 1015, and contained pus and albumin, but no blood. A stone was detected on sounding the bladder. I operated on August 5th. The bladder held only 3 ounces of fluid, and the stone proved too large to be properly grasped by the lithotrite with this small distension.

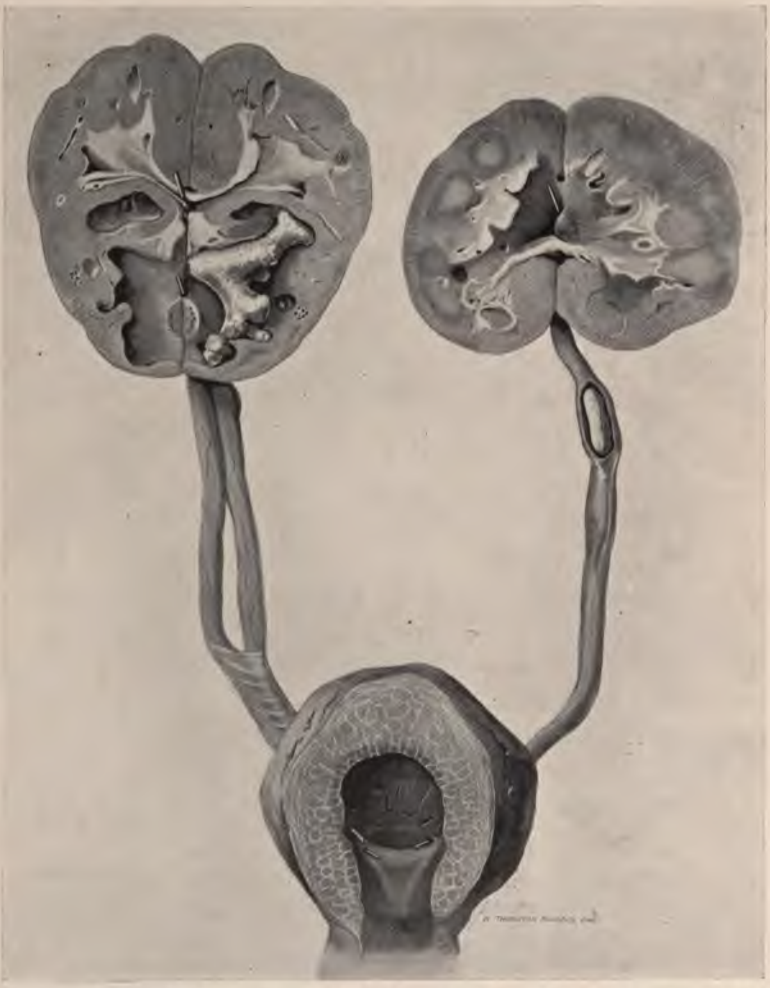

PLATE IV.—Kidneys, ureters and bladder in case of septic pyelonephritis complicating vesical, ureteral and renal calculi. Chronic cystitis and hypertrophy of bladder. Double right ureter draining upper and lower halves of kidney. Lower half of right kidney destroyed by calculus, upper half shews recent pyelonephritis. Calculus in left ureter. Commencing distension of left kidney.

I therefore made a median perineal opening upon a grooved staff. The forceps grasped the stone readily, but it was found impossible to remove it by this means. An attempt to crush the stone through the perineal wound with a lithotrite failed, and I therefore opened the bladder suprapubically and extracted the calculus. The patient made a good recovery from the operation, and the drainage tubes were removed on the 13th day. The urine remained foul in spite of the daily irrigation of the bladder. The temperature rose to 99° for two days after the operation, and after that was subnormal (Chart 4, p. 26).

A fortnight after the operation the patient's appetite failed, and there was some nausea and a little retching, but this subsided, and he took his food better. He began to lose flesh, however, and rapidly became emaciated and sallow. The abdomen was repeatedly examined, but no tenderness or enlargement of the kidneys was found. The temperature was persistently subnormal throughout. He died suddenly four weeks after the operation.

Post-mortem, the bladder was found contracted, and was the seat of chronic cystitis (Plate IV.).

The left kidney shewed pyelonephritis, and was not dilated. In the left ureter a calculus the size of a hazel nut was impacted about an inch above the brim of the pelvis.

The right kidney was large, and was drained by two ureters which emerged from two separate pelves and were united by areolar tissue. The segments of the two ureters below the brim of the pelvis were more firmly united. The ureters opened separately into the bladder in the usual position of the right ureteral opening. The duct draining the upper part of the kidney opened above and behind that draining the lower part.

The lower part of the right kidney was extensively destroyed by a large branching calculus. The pelvis of the upper portion of this kidney was dilated and shewed recent pyelitis. The whole kidney was in a condition of chronic septic pyelonephritis.

EXPOSURE OF THE KIDNEYS BY OPERATION TO ESTIMATE THE RENAL FUNCTION

I shall not consider palpation of the kidneys after opening the peritoneal cavity, for the results of this method of examination have been found to be unreliable.

The exposure of the kidneys by lumbar incision with a view to estimating their functional activity, where this is in doubt, subjects the patient to a risk which cannot be considered advisable. Nephrotomy performed for the purposes of diagnosis has been followed by suppression of urine and death when the kidney explored was the healthy organ whose neighbour had been destroyed by tuberculous disease.

And, moreover, it is not always easy to judge of the functional power of a kidney so exposed. This was impressed upon me in a case already related (Case 3, p. 9), where suppression of urine had followed an operation for stricture, and I cut upon one kidney and stripped its capsule in the hope of relieving the tension that is supposed to exist in these cases. The kidney was flabby, and except for venous congestion did not differ in appearance, size, or consistence from a fully functional kidney.

It is possible that some means may yet be developed by which actively functional kidney tissue can be recognised on exposing the organ.

In a case of exploration of the kidney where I had used the methylene blue test for the purposes of diagnosis, and where the blue colour of the urine was still strongly marked, I hoped to find, on incising the kidney, that the exposure to air would produce the blue colour observed in animals that are passing methylene blue. I should then have been able to recognise the extent of the fibrous changes in the renal substance by variations in the staining. I was disappointed, however, for no change in colour was observed. Nor did the use of peroxide of hydrogen as an antiseptic during the operation bring out the colour as it would have done in a urine containing the leuco-derivatives of methylene blue.

CHAPTER II

EXAMINATION OF THE URINE

Chemical composition of the urine—Variations due to extrarenal influences—Urea—Chlorides—Quantity of urine—Polyuria—Oliguria—Anuria

I.—CHEMICAL EXAMINATION OF THE URINE

MUCH importance has been attached to the chemical analysis of the urine in estimating the activity of the kidneys. The quantity of urea and chlorides and the presence of albumin and other abnormal substances in the urine have been considered of most importance in this estimation.

The composition of the urine is dependent upon too large a number of extrarenal factors for absolutely reliable conclusions in regard to the function of the kidney to be based upon a quantitative analysis of the fluid. The amount and composition of the food, the activity of metabolism, the functional state of the liver and to a less degree of other glands, are factors which give rise to changes in the chemical composition of the urine. To correct such influences the mixed urine of 24 hours is examined, and a diet of carefully estimated composition may be given and the intake of fluid controlled. Such precautions are essential, but it is not always possible to carry them out.

But even where the examination can be made under such favourable conditions, there are other fallacies which may vitiate the result.

Diseases of other organs, such as the liver, may alter the composition of the urine passing through a normal kidney. The feverish state brought about by some surgical diseases of the kidneys, or arising from conditions apart from the urinary tract, will cause changes in the amount and composition of the urine which will interfere with an accurate estimation of the renal activity. The discovery of albumin and other abnormal substances in the urine is important in diagnosis, but does not give information in regard to the functional activity of the kidneys. I shall consider variations in the quantity of urea and chlorides in greater detail.

Urea.—The average quantity of urea excreted in the urine in 24 hours in a healthy individual is about 33 grammes (500 grains), or, relatively to the quantity of urine passed, 2 per cent.

The quantitative estimation of urea has been relied upon for information in regard to the renal activity.

It is recognised that the excretion of urea is diminished in organic diseases of the kidneys. This is generally accepted as occurring in Bright's disease, and it has been carefully studied in relation to surgical diseases of the kidneys by Albarran.* This observer has shewn that in unilateral renal disease the urea is diminished in amount in the urine of the diseased kidney when compared with the healthy organ. As both kidneys receive an equal quantity of urea from the blood, the analysis of the urine of each will shew the comparative activity of each organ in excreting it. This observation is therefore of value where the function of the two kidneys is to be compared. But where the blended urine from the two kidneys is being examined it is impossible to say how much a reduction of the urea may be due to kidney disease and how much to other causes.

The extrarenal causes for variation in the urea output are many. The urea found in the urine is dependent very largely upon the proteid of the diet. An increased meat diet will produce an increased elimination of urea in the urine, and a diminished proportion of meat in the food has the opposite effect. A non-proteid diet does not, however, result in the complete disappearance of urea from the urine, and a certain proportion of the urea is derived indirectly from metabolism in the tissues. Urea is formed in the liver, and probably to a small amount also in other glands.* The supply of urea which arrives at the kidney for removal is therefore a variable one, depending upon diet, absorption, tissue metabolism, and hepatic action. Any one of these processes may be affected by disease.

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* Guyon and Albarran, Assoc. française d'urologie, 1897, p. 11.

Apart from the functional power of the kidney to excrete urea, renal disease may indirectly bring about variation in the urea output by interfering with assimilation or by increasing or diminishing metabolism. The difficulty with which the subjects of advanced surgical renal disease take solid food is one of the striking features of the disease, and this affects the output of urea by cutting down the supply of proteids. The feverish state which results from many diseases of the kidneys will cause increased metabolism, and augment the quantity of urea which must be excreted.

The effect of renal disease upon the tissue metabolism apart from these factors is beyond the scope of this investigation, but it cannot be doubted that in advanced renal disease very profound metabolic changes proceed *pari passu* with the renal lesion, and the effect of these upon the urea output must be considerable.

Maragliano† and Licci‡ go further, and state that the diminution of urea in cases of renal disease is entirely due to disturbances of the nitrogenous metabolism. The renal permeability to urea and other azotised products is, they say, increased rather than diminished.

These authors hold that in nephritis those of the azotised products, which are less dialysable than urea, and which in the normal state traverse the kidney in small quantities, pass readily through the altered epithelium. Thus the proportion of azotised bodies in the form of urea, which is normally 80 per cent. of the total azotised bodies, may be reduced to 70 per cent.

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* Munzer, *Archiv. f. Pathol. u. Pharmak.*, 1904, Bd. xxxiii., S. 164. Kaufmann, *Archiv. de physiol. norm. et path.*, 1894, p. 531.

† *La Clinica Medica Italiana*, 1902, p. 437.

‡ *Il Policlinico*, 1901, p. 400.

The urea output thus bears a variable relation to the total excretion of nitrogen, and, if observations are to be made upon the nitrogenous output, it must be considered as a whole.

Folin * has made a careful study of the nitrogen distribution in 30 normal urines, the daily nitrogen in which ranged from 2.7 to 16 grammes. The following figures are extracted from this writer's tables :—

Relation of the Nitrogen in the various Nitrogen Compounds of the Urine to the total Nitrogen.

Total nitrogen in grammes	5	7	9	11	13	15
Percentage of total nitrogen as NH_3 nitrogen .	6.4	3	4.4	3.5	3.6	3.6
Percentage of total nitrogen as urea nitrogen .	73	80	80	83	84	86
Percentage of total nitrogen as ammonia and urea nitrogen	76	84	84	86	87.6	89
Percentage of total nitrogen as kreatinin nitrogen	12	8	6.1	5.5	5.4	5.1
Percentage of total nitrogen as uric acid nitrogen	3	2	1.6	1.3	1.6	1.2
Percentage of total nitrogen as undetermined nitrogen..	8	6.9	7.3	6.7	5.1	4.0

It will be seen from these figures that the supply of urea with which the kidney has to deal represents a variable proportion of the total nitrogen excretion, and that, within the limits of health, oscillations may occur without any profound disturbance of metabolism being present. With this inconstant supply of urea to the kidneys, the excretion of this body must form a very unreliable guide to the function of these organs.

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* *Amer. Jour. of Physiol.*, 1905, xiii., p. 45; also *Zeitschr. f. physiolog. Chem.*, 1901, xxxii., S. 504.

Chlorides.—Most of the chlorine in the urine is in the form of chlorides, of which chloride of sodium forms the major part.

From 6 to 10 grains of hydrochloric acid are excreted by a healthy adult on ordinary diet.

A constant sodium chloride content is maintained in the tissues and fluids of the body. The supply is obtained from the food, and any diminution of the supply is followed immediately by a diminution of the output. The absorption of chloride of sodium appears to stimulate metabolism, whether the kidneys are healthy or diseased.*

The chlorides in the urine are diminished to a remarkable degree in fevers, and there is an excessive elimination after the temperature has fallen. A similar reduction of the quantity of the chlorides in the urine has been observed in various states where effusion is proceeding, and an excessive elimination takes place when the effusion is in process of absorption.

In acute nephritis there is retention of chlorides; in chronic nephritis, according to Mohr,† the chlorides in the urine are in excess. In acute exacerbations occurring in the course of chronic nephritis and during uræmic attacks the chlorides are diminished.

Coincidently with a diminished chloride output the quantity of urea is usually reduced, but the excretion of these bodies may not run parallel, as Widal ‡ has noted in Bright's disease, and Albarran § has demonstrated in surgical diseases of the kidneys.

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* Claude et Villaret, *Bull. de la Soc. de Biol.*, 30 Mai, 1904. Claude et Mauté, *Bull. de la Soc. méd. des hôp.*, 2 Mai, 1902.

† *Zeitschr. f. klin. Med.*, 1904, S. 331.

‡ *Bull. de la Soc. méd. des hôp.*, 1903, p. 990.

§ "Exploration des fonctions rénales," 1906.

The latter observer found, in comparing the output of chlorides by each kidney when one organ was diseased, that they were constantly reduced on the diseased side. Usually, he found that the elimination of chlorides and urea pursued a parallel course; in some cases they were dissociated. He gives the following table of results of his observations in cases of unilateral renal disease :—

	CASES
Proportion of urea and chlorides almost similar on the two sides	8
Proportion of chlorides higher than that of urea, but affected similarly	91
Proportion of chlorides lower than that of urea	24

Albarran concludes that "the elimination of chlorides in the urine passed during twenty-four hours does not furnish a precise indication of the activity of the renal function ; from this point of view it is of less importance than the elimination of the azotised bodies."

No reliable information has been obtained in regard to the renal function from the observation of the phosphates or of the uric acid of the urine.

II.—QUANTITY OF THE URINE

Polyuria.—The quantity of urine passed by a healthy individual in 24 hours amounts to from 1,200 to 1,500 cubic centimetres. Considerable variation may take place, depending upon the removal of water from the body by the skin, lungs, intestines, etc., the amount of fluid ingested and other physiological factors, so that the amount may fall to 800 or 900 c.c., or rise to 1,800 c.c.

Polyuria may result from a large number of causes, some of which are transient, such as the polyuria of an epileptic attack, or the critical polyuria at the end of a fever, while others are continuous, as in the polyuria of cardiac disease and the various forms of diabetes.

The form of polyuria which is important to the present investigation is that which accompanies certain diseases of the kidneys. The diagnosis of this from other forms of polyuria is not in question. These remarks must refer merely to the value which polyuria assumes in an attempt to estimate the renal function in a case of surgical disease of the urinary organs. Here an increase or a diminution of the quantity of urine passed may be of grave import, for either may be a sign of reduced renal activity.

1. It is said that an increased frequency of contraction of the bladder will increase the volume of the urine. "The more frequently the bladder contracts, the more active becomes the urinary secretion. Even under normal conditions it is possible, by frequently passing water voluntarily, to increase the quantity of urine, and in all forms of disease where there is increased desire and frequency of micturition, there is as a rule also an increased quantity of urine." *

From this point of view the polyuria that accompanies enlargement of the prostate may in some measure be due to reflex diuresis. But it can only in part depend upon this factor.

2. Polyuria is a constant symptom in chronic interstitial nephritis, and much speculation has arisen as to the true cause of the phenomenon. The renal disease has been looked upon both as the cause and as the effect of the accompanying high arterial tension. The kidney which is in process of destruction by increased pressure from urinary obstruction has the anatomical characters of interstitial nephritis in addition to the hollowing of the organ. Such kidneys continuously discharge large quantities of watery urine, whether the bladder contracts frequently or not at all. In such patients the arterial tension is not raised ; on the contrary, it is frequently lowered.

Whatever may be the cause of this polyuria, it is a

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* O. Zuckerkandl, in "Handb. d. Urologie," Frisch u. Zuckerkandl, Bd. i., S. 775.

significant phenomenon in urinary obstruction. The percentage of urea and of other urinary constituents is much reduced. The total quantity of these bodies passed during twenty-four hours may be only slightly below the normal standard or may be much reduced.

In a patient suffering from enlarged prostate who came under my care at St. Peter's Hospital, the quantity of urine passed during 24 hours varied from 70 to 100 ounces or more, had a specific gravity of 1005, and shewed a faint cloud of albumin. There was 0.6 per cent. of urea in 108 ounces passed in 24 hours (Chart 5).

This patient had suffered from distension of the bladder with overflow for 12 months, and had begun to use a catheter a month before I saw him. Suppression of urine followed the operation of prostatectomy. I have already (p. 6) described the gross and microscopical changes in the kidneys in this case.

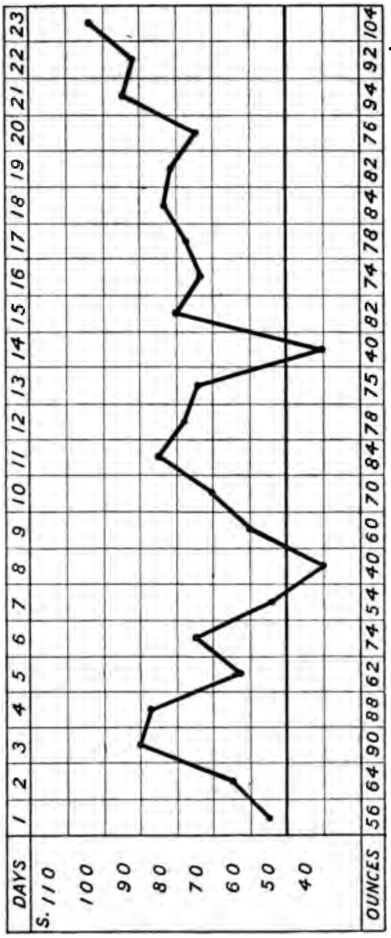

Chart 5.—Urine chart in case of enlarged prostate with polyuria.

The polyuria of urinary obstruction points to a serious lowering of the renal activity, and, as in the case to which I have just referred, suppression of urine frequently follows surgical interference where it is a prominent symptom.

The relief of the obstruction may react on such kidneys in one of two ways. Either the polyuria becomes less pronounced, or the urine becomes totally suppressed. The rapid withdrawal of large quantities of urine from the bladder in a case of this nature when the patient is suffering from retention of urine causes suppression of urine in a certain proportion of cases.

The more gradual relief of urinary tension is less likely to be followed by cessation of the secretion, and if the pressure be maintained at a low degree over a considerable period of time by drainage of the bladder, the urinary secretion appears to regain its balance and to approach more nearly the normal standard. What changes take place in the renal tissue or in the circulation within the organs I am unable to state, but it is certain that the functional activity of the kidneys is more stable and better able to withstand the strain of an operation for the permanent relief of the obstruction. Thus, in the case of a patient suffering from an enlarged prostate with a distended bladder from chronic retention, the safest method of treatment, so far as the function of the kidney is concerned, is a gradual emptying of the bladder extending over several hours, followed by continuous catheter drainage and after a time by cystotomy. The operation of prostatectomy would be performed after an interval of some weeks. Such was the method of procedure in the case of G. B. which I shall presently relate (p. 110), and it was successful under most adverse conditions.

In other cases, a polyuria is said to follow the relief of urinary tension, as, for example, after the relief of vesical retention or the re-establishment of a passage in hydronephrosis (Zuckerkandl).*

In cases where advanced calculous disease has reduced the kidney tissue to a mere shell the secreting substance is still further reduced by the presence of chronic interstitial nephritis. In these cases a continuous polyuria is observed, and its presence is an indication of a greatly reduced renal function.

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* "Handb. d. Urologie," Frisch u. Zuckerkandl, Bd. i., 1904.

There remain for consideration several types of case where polyuria is temporary.

3. Polyuria may alternate with periods of oliguria. The accompanying chart (Chart 6) is a record of the quantity of urine and the temperature in a case of pyelonephritis which followed the operation upon a longstanding stricture complicated by periurethral abscess. It will be seen that in this chart there are alternating periods of diminished urine (10 to 30 ounces), and polyuria (70 to 106 ounces), and that the oliguria coincided with the recurrent exacer-

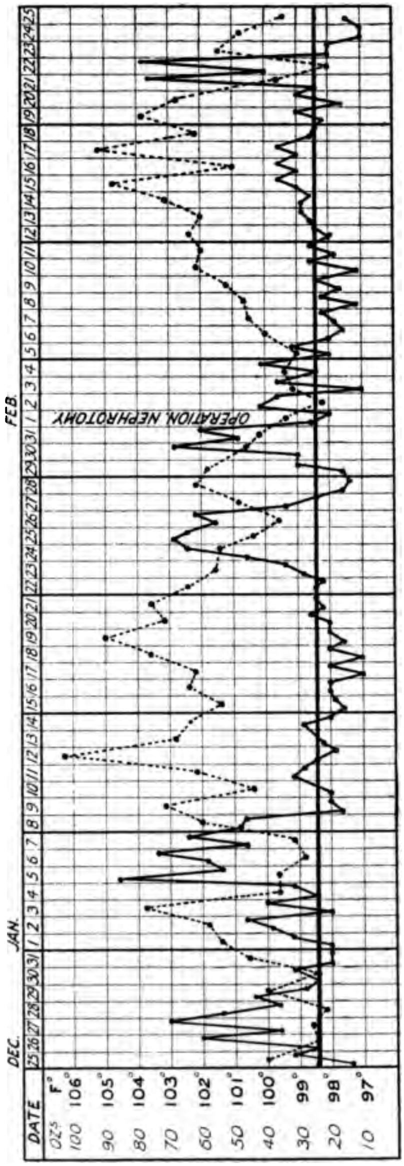

Chart 6.—Temperature (continuous line) and quantity of urine (dotted line) in a case of chronic suppurative pyelonephritis with acute exacerbations. Polyuria and a normal or subnormal temperature alternate with oliguria and fever.

bations of the suppurative pyelonephritis, while the polyuria was observed in the intervals when the temperature was normal or subnormal.

4. Polyuria of temporary duration usually follows the removal of a kidney the seat of advanced disease, where the remaining kidney is sufficiently healthy to carry on the renal function (Charts 7 and 8).

This polyuria might be ascribed to the reduction of the total renal tissue by the nephrectomy, for it has been shewn by Dr. J. Rose Bradford that polyuria follows upon the removal of portions of the kidneys in animals. In the human subject, however, many of these kidneys before removal were entirely destroyed by disease, and it seems much more likely that this polyuria is the reaction following upon the relief from an inhibitory reno-renal reflex.

5. Lastly, there is the transient polyuria which frequently interrupts the course of obstructive anuria (Chart 1, p. 8). The sudden transition from complete suppression to the flow of great quantities of urine for a short period of time, immediately succeeded by complete suppression of the secretion, appears at first sight to be something of the nature of a paradox. For it seems as if the kidney alternated between extreme activity and complete paralysis. This is not so. Polyuria of this nature is the nearest functional approach to absolute suppression of urine. The patient who is passing the greatest quantity of urine in surgical diseases of the kidneys is nearest to complete anuria.

Oliguria, anuria.—A diminished secretion of urine is oliguria, a total cessation of secretion is anuria. No complete discussion of this significant sign is possible here. It will be considered very briefly, and only so far as may indicate its significance in surgical diseases of the urinary organs.

In surgical affections of the urinary organs the passage of a quantity of urine much below the normal standard

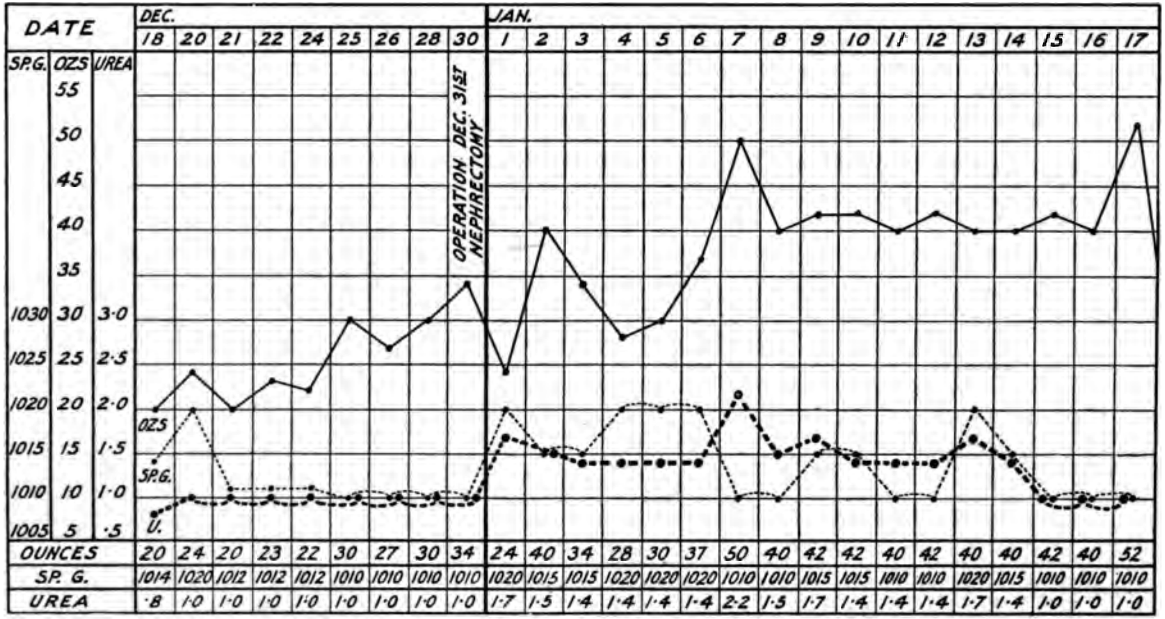

Chart 7.—Increased secretion of urine with raised specific gravity and percentage of urea following nephrectomy in case of calculous pyonephrosis.

DATE	DEC. 18	20	21	22	24	25	26	28	30	JAN. 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
OUNCES	20	24	20	23	22	30	27	30	34	24	40	34	28	30	37	50	40	42	42	40	42	40	40	42	40	52
SP. G.	1014	1020	1012	1012	1012	1010	1010	1010	1010	1020	1015	1015	1020	1020	1020	1010	1010	1015	1015	1010	1010	1020	1015	1010	1010	1010
UREA	·8	1·0	1·0	1·0	1·0	1·0	1·0	1·0	1·0	1·7	1·5	1·4	1·4	1·4	1·4	2·2	1·5	1·7	1·4	1·4	1·4	1·7	1·4	1·0	1·0	1·0

is usually significant of grave interference with the renal function.

Some consideration must, however, be given to the circumstances under which the lowered secretion takes place. High fever, reduced absorption of fluid, profuse sweating, diarrhœa, and other causes of reduction of the body fluids may complicate urinary disease, and lead to a diminished quantity of urine.

Some individuals of slight build and spare habit constantly have a small urinary output. In a young lady whom I examined in consultation with Dr. Fourneaux Jordan, of Birmingham, the usual urinary secretion was below 10 ounces in 24 hours. In Dr. Fourneaux Jordan's words, " For three weeks before operation (with the exception of two days far apart when the quantity rose to 18 ounces), she passed 8 to 10 ounces, on one occasion the quantity was as small as 7 ounces." On three consecutive days the amount of urea was 2.3, 2.6, and 2.1 per cent. This patient suffered from frequent attacks of intense renal pain which eventually recurred every twelve hours. The kidney had been operated upon twice previously, once on account of undue mobility, for which a nephropexy was performed, and once on account of pain and hæmaturia, when a small stone was removed from one of the calyces. After a prolonged operation, in which I explored the kidney and ureter, there was no subsequent oliguria. The dressings were soaked with urine a few hours after the operation, and the total urinary secretion rapidly returned to the original quantity.*

1. It has already been noted that urinary obstruction may be accompanied by polyuria, from interstitial changes in the kidneys, and the same is observed in chronic interstitial nephritis due to other surgical diseases of the kidneys, such as stone. In such a case a rapid diminution of the quantity of urine secreted is a sign of renal failure, and

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* A recurrence of the pain afterwards necessitated nephrectomy.

may be preliminary to a total cessation of function. This sudden collapse of a polyuria is seldom brought about by extra-urinary agencies; but occasionally some influence, such as exposure to cold, may lead to the suppression of the renal function. Usually the oliguria or anuria follows surgical interference with the urinary tract, such as the passage of a catheter or bougie.

2. In cases of sepsis of the urinary tract, where an ascending infection of the kidneys (pyelonephritis) has occurred, a diminished renal secretion is the rule. This is the last phase of many forms of surgical disease of the lower urinary organs, such as malignant growths of the bladder which have not occluded the ureters, chronic cystitis from recurrent stone, etc. Small quantities of ammoniacal urine containing pus, blood, and *débris* are passed frequently. The total quantity of urine is reduced and complete anuria may at any time supervene. More often, however, the function is not completely suppressed when uræmic symptoms appear, and small quantities of urine are secreted up to the time of death. The combination of obstruction with this state, as in cases of enlarged prostate or stricture, may lead to polyuria with recurrent attacks of oliguria (*see* Chart 6, p. 41). Usually, however, the quantity of urine is continuously diminished.

3. The reflex effect of irritative lesions of the urinary tract upon the renal function is generally recognised. It is illustrated in cases of the passage of a calculus along the ureter by the temporary reduction or even complete suppression of urine. The oliguria or anuria of these cases is often transient. It ceases when the attack of colic is past, and is frequently followed by a temporary polyuria.

Complete anuria is more often due to nephrolithiasis than to any other single cause. Both ureters are rarely blocked by calculi; usually a calculus suddenly obstructs the ureter of a kidney whose neighbour has previously been destroyed by disease. Or a stone is suddenly arrested in the ureter and causes suppression of the function of the corresponding kidney by blocking the duct, and of the second kidney by reflex uretero-renal inhibitory impulses.

4. Oliguria and even complete anuria may be caused by reflex impulses acting on one kidney and originating in its diseased neighbour.

Israel records the case of a young man with an intermittent hydronephrosis on the right side due to kinking of the ureter of a movable kidney. From time to time great distension of the kidney caused intense pain. During these attacks the secretion of urine was reduced to a minimum, while the emptying of the sac by puncture re-established the flow of urine. For the first two days after the puncture an abundant polyuria replaced the anuria, and was distinguished as coming from the healthy kidney because it was not bloodstained like the fluid removed from the hydronephrosis. After about ten days the urine regained its normal quantity and colour.

In each of two further cases of anuria* due to the obstruction of one ureter by stone, the second ureter was free from obstruction, and the kidney was functionally active previous to the onset of the anuria.

This observer also relates a case in which he looked upon the pressure of a drainage tube upon the renal pedicle after nephrectomy as the cause of an anuria, which was succeeded by copious polyuria on removing the cause of the irritation.

It is said that surgical interference with one kidney may reflexly cause anuria by suppressing the function of the other. It would be difficult to bring forward direct evidence in support of this view. There are many other conditions which may produce anuria after an operation upon one kidney. The amount of urine secreted by the second kidney is constantly diminished after such operations, but it does not appear to be much more so than in severe operations upon other organs. When the second kidney is previously healthy the factors of shock, loss of blood, absorption of antiseptics, and the influence of the circulating anæsthetic must be considered, and when the

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* Meyer, *Annals of Surgery*, 1892. König, quoted by Israel, "Nierenkrankheiten," 1901.

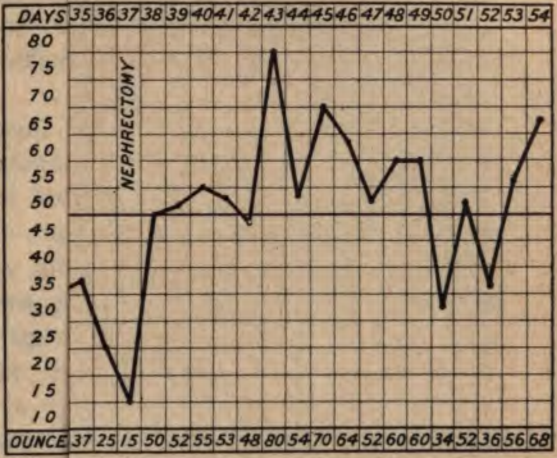

Chart sis. Nephrectomy was followed by an increased

first kidney. Yet it is difficult to bring forward an undoubted case of the effect of this reflex stimulus.

Chart 8 shews the quantities of urine passed each twenty-four hours during 54 days in a patient aged 57 years. This man suffered from stricture of the urethra, for which the operation of internal urethrotomy was performed. It was then found that he had a large pyonephrosis on the left side. This was drained by nephrotomy, and 14 days later the pyonephrotic kidney was second kidney is constantly diminished after such operations, but it does not appear to be much more so than in severe operations upon other organs. When the second kidney is previously healthy the factors of shock, loss of blood, absorption of antiseptics, and the influence of the circulating anæsthetic must be considered, and when the kidney is already diseased these factors will assume an even greater importance. When nephrectomy has been performed a diseased second kidney may have been previously incapable of carrying on the renal function, and the removal of the more diseased kidney only brings into prominence the inefficiency which existed before the operation.

On the other hand, it is a frequent observation that where a kidney distended with pus or urine is incised, or where a diseased kidney is removed and the second kidney is efficient, a rapid improvement in the secretion of urine takes place after a transient depression of the function. For a time polyuria often takes the place of the pre-operative oliguria. The depressant action of a diseased kidney upon the function of its healthy or less diseased neighbour is well illustrated by these cases.

If surgical interference with the kidney were in itself a powerful factor in the production of reflex anuria, this condition might reasonably be expected to occur in a fair percentage of cases, and shew some relation to the gravity of the operation which was performed upon the first kidney. Yet it is difficult to bring forward an undoubted case of the effect of this reflex stimulus.

Chart 8 shews the quantities of urine passed each twenty-four hours during 54 days in a patient aged 57 years. This man suffered from stricture of the urethra, for which the operation of internal urethrotomy was performed. It was then found that he had a large pyonephrosis on the left side. This was drained by nephrotomy, and 14 days later the pyonephrotic kidney was removed. The average quantity of urine during 17 days before the nephrectomy (excluding the day of the nephrotomy, on which only 8 ounces of urine were passed) was 36 ounces, and for 17 days after the removal of the kidney it was 55 ounces. No cause of increased secretion other than removal of the suppurating kidney could be discovered. The quantity of urea and the specific gravity of the urine is increased during the polyuria in such cases. This may be seen in the chart of the urine before and after nephrectomy for advanced calculous pyonephrosis (Chart 2, p. 43).

Anuria may follow operations upon the lower urinary tract, and although some of the causes of this have already been mentioned in a general way, it is convenient to bring them together in this relation. It may arise in the following ways :—

1. From the sudden relief of urinary obstruction.
2. By reflex vascular or secretory influences.
3. By the absorption of virulent poisons.
4. By ascending inflammation.

The effect of the sudden relief of obstruction has been referred to under the heading of polyuria. It may be further noted that the interference with the renal function which follows this procedure is more frequently met with in the aged than in young men, in the retention of enlarged prostate than in the retention of stricture of the urethra. The cause to which the anuria is ascribed is the sudden change in intrarenal pressure which disturbs the vascular arrangements of the kidney, and, by engorging the kidney with blood, interferes with the secretion of urine. The different position of the obstruction in the case of stricture and enlarged prostate does not appear to explain the frequency of the anuria in the one as compared with the other. The factor of age is that which is most striking in comparing the two classes of case, and it is probable that the difficulty with which the circulation accommodates itself to changes of pressure in old men may account for the incidence of anuria.

It is beyond the scope of this investigation to enter fully into the question whether the suppression of urine which may follow the passage of an instrument through a stricture, or the incision of a stricture, when the kidneys are apparently healthy is due to reflex influences on the secretory or vascular mechanism of the kidney, or whether it results from the absorption of poisons from the urethra, although a few words must be said on this point.

That reflex vascular and secretory effects may be produced by irritative lesions of the lower urinary tract is admitted by everyone. In the case of J. F. (p. 11), I have related a very striking example of this. The patient had recovered from a severe attack of cystitis and pyelonephritis, for which cystotomy and nephrotomy had been performed. The cystotomy wound was explored with the finger, and suppression of urine immediately followed and continued for 15½ hours. There was some hæmorrhage from the nephrotomised kidney, shewing that congestion of the kidney was a factor in the anuria. And further, the urine which had discharged from the nephrotomy wound ceased with the advent of anuria, and did not commence again until some hours after the flow of urine from the bladder was re-established, which shewed that the severely damaged kidney did not resume its function until some time after its more healthy neighbour.

The point which is at issue is whether these cases of suppression following an operation such as internal urethrotomy with previously healthy kidneys are to be placed in this category.

The most cogent argument against such a reflex being the whole cause of the fatal disease is that, if the secretory function of the kidneys is inadvertently brought to a sudden close by other means, such as the removal of a solitary kidney, the train of symptoms which

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follows resembles that of calculous anuria, and completely differs from that which follows in the cases now under consideration.

A part of the reflex theory is the view that the kidney becomes so engorged with blood by the reflex effect that, bound within its fibrous capsule, the circulation within the organ ceases, and with it the secretion. According to this view the kidney should be tensely distended with blood, and incison of the capsule should relieve this condition.

Acting on this belief, I endeavoured by stripping the capsule of the kidney in such a case to relieve the circulation of the organ. I did not find that the supposed distension of the kidney existed, and the attempt to relieve the anuria proved unsuccessful. This case presented the usual symptoms which accompany the suppression of urine in these cases. There was the initial rigor, sudden rise of temperature, which was maintained, early restlessness followed by muttering delirium, drowsiness and rapid sinking into coma, the progressive failure of the circulation, and death within a few hours of the rigor and without convulsions or other signs of uræmia.

It would be difficult to reconcile such a case as this with the theory of reflex suppression. The whole picture is that of a virulent poison absorbed into the circulation. It seems probable that in such cases the suppression of urine is only part of a general condition of suspended function, and is not in itself the origin of the intoxication. It is difficult to say what the significance of the engorgement of the renal vessels may be. The appearance of the kidney does not differ greatly from that found in other acute intoxications, with the exception that the renal epithelium does not appear to suffer.

There are many cases of a somewhat similar nature which differ only in degree, and which react to the vigorous application of diuretic, diaphoretic, and cathartic measures. These patients recover after an oliguria accompanied by high fever, with some tympanitic distension of the abdomen which lasts for a few days.

An ascending septic infection of the kidneys may be unilateral or bilateral. Its intimate relation with the passage of surgical instruments has led to the term "surgical kidney" being used for this form of pyelonephritis. It is frequently but not necessarily combined with urethral obstruction. The diminution of the urine in such cases will vary according to the degree of the pyelonephritis, and whether it is unilateral or bilateral in its distribution.

It is seldom that complete suppression of urine takes place in these cases, even where a fatal issue supervenes.

CHAPTER III

THE KIDNEY AS A FILTER

Physiology of the Renal Function—Cryoscopy of the Urine—Cryoscopy of the Blood—Method of Wright and Kilner—Electrical Resistance of the Urine and Blood—Surface Tension of the Urine

ALTHOUGH it cannot be said that all the facts in the physiology of the renal function are fully known, certain phenomena are recognised as being either a part of the function or inseparably connected with it. The methods that have been recently introduced for the purpose of estimating the value of the renal function in surgical diseases consist in the examination of these phenomena and in noting the modifications produced in them by disease.

1. The kidneys separate from the blood a fluid of different molecular composition—namely, the urine.

The osmotic pressure of the urine is greater than that of the blood, and the work performed by the kidney may be measured by estimating the osmotic pressures of the two fluids.

This is conveniently done by investigating the freezing point of these fluids (cryoscopy).

2. The kidneys exercise a selective power by which certain substances are removed from the blood. Thus certain of the constituents of the urine do not appear in other secretions of the body, although they circulate in the blood.

In similar manner certain foreign substances introduced into the blood are eliminated by the kidneys. Thus iodide of potash, salicylate of soda, and other drugs are passed out in the urine, and certain dyes, such as methylene blue, fuchsin, and rosaniline may be recognised in the urine by the changes in colour which they produce. The kidneys are also credited with the power of removing certain toxic bodies from the circulation, the accumulation of which would produce the syndrome of uræmia.

3. It is further recognised that the kidneys have a synthetic action in regard to at least one substance which exists in small quantities in the urine, and in this way they are brought into line with glandular organs. Thus the kidney can manufacture hippuric acid from glycin and benzoic acid. Again, it is known that the administration of phloridzin is followed by the temporary appearance of glucose in the urine, and that the glucose is produced by the vital action of the kidney.

4. Finally, a controlling function over nitrogenous metabolism by means of an internal secretion has been suggested by certain experiments.

ESTIMATION OF THE FREEZING POINT OF THE URINE AND THE BLOOD

CRYOSCOPY

If a layer of distilled water be superimposed upon a concentrated solution of a coloured salt (say sulphate of copper), the colour will be seen to pass gradually into the clear water until the whole fluid is equally coloured. A certain power moved the molecules of the coloured solution into the water. This movement of molecules is termed **diffusion.** Diffusion always takes place from fluids of a higher concentration to those of a lower until the whole is equally concentrated.*

If the solution and the water are separated by a wall which allows of the passage of water but not of the salt molecules, the molecules will exert a certain pressure upon the wall. This is called the **osmotic pressure** of the fluid. In order to demonstrate this process a wall must be obtained which is permeable to water, but not to substances dissolved in water. These are "semi-permeable membranes," and were first made artificially by Traube, who named them "precipitation membranes" from the method of their manufacture.

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* Koeppe, in "Handb. d. Urolog.," Frisch u. Zuckerkandl, Bd. i., 1904.

Pfeffer* succeeded in measuring the osmotic pressure of solutions of cane sugar by such a membrane, and found that the osmotic pressure was proportional to the concentration of the solution. The osmotic pressure is independent of the nature of the dissolved material.

Van t' Hoff shewed that this osmotic pressure of a solution was proportional to the number of molecules contained, and was related to certain other properties, such as the lowering of the freezing point and of vapour tension and the elevation of the boiling point.

Since these properties of a solution are proportional, it is only necessary to determine one of them in order to estimate the others. By this means a ready method of measuring the osmotic pressure of any fluid was obtained.

The estimation of the molecular contents of physiological fluids by ascertaining the boiling point is unsuitable, as certain changes are produced by heat which disturb the molecular concentration. Thus Landsberger† has shewn that Beckmann placed the molecular weight of the urine, as shewn by the boiling point, too high—namely, at 72° to 74°, instead of at 60° C.

There remains, however, the method of estimating the lowering of the freezing point (cryoscopy) as a means of measuring the osmotic pressure or the molecular content of the urine.

According to Ludwig's theory (filtration) of the secretion of urine the osmotic pressure of urine might balance, but could never exceed, that of the blood. But, as Dresser* has pointed out, the osmotic pressure of the urine is considerably in excess of that of the blood. This work of extracting from the blood a fluid of greater osmotic pressure is performed by the healthy kidneys, but if the kidneys are diseased, their power of bringing about a change in the osmotic tension of the fluid passing through is reduced. The osmotic pressure of the urine then falls and approaches more nearly that of the blood. The molecular content of the urine is reduced and the freezing point of the urine is raised.

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* "Osmotische Untersuchungen," Leipsig, 1877.

† *Berichte d. deutsch. chem. Gesellsch.*, Bd. xxxi., S. 4, 1898.

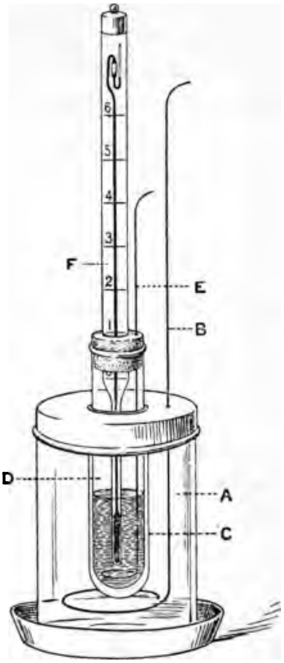

Fig. 2.—Beckmann's apparatus for estimating the freezing point of the urine.

A, glass jar; B, stirring rod; C, outer glass tube; D, inner glass tube for urine; E, platinum stirring rod; F, Beckmann's thermometer.

Method.—I have used the apparatus of Beckmann†, but there are other varieties which are equally satisfactory‡ (Fig. 2). It consists of a glass jar with cover A, to hold the freezing mixture. In this is placed a glass tube C, within which is a second tube D containing the urine. This second tube is fitted with a cork supporting a Beckmann's thermometer F, and a platinum stirring rod E. The outer tube acts as an air mantle. The scale of the thermometer covers 5° to 7° C., and each degree is subdivided into 100 parts. The thermometer is prepared for use in the following manner. The quicksilver of the reservoir is added to the upper part by inverting the thermometer and tapping

* *Archiv. f. exp. Pathol. u. Pharmak.*, 1892, Bd. xxix., S. 307.

† Ostwald, "Grundriss der allg. Chem.," Leipsic, 1899.

‡ Jouffray recommends the apparatus of Chanoz; Albarran that of Bousquet.

it gently. The bulb of the thermometer is then placed in water which is slightly above the freezing point, and the thread of mercury shrinks. By a sharp tap the excess of mercury which was hanging above the reservoir falls down into it, away from the upper end of the mercurial filament. The bulb is now placed in water which is brought to the freezing point, and the mercury shrinks until it rests at a certain point on the scale. On removing the bulb from the freezing water the mercury will rise and a portion hanging over the reservoir will again appear. In order that this may not be detached and necessitate the readjustment of the instrument, the thermometer should be carefully handled, and should be clamped to an upright. The glass jar is now filled with a mixture of finely crushed ice and salt, and the outer tube placed in the mixture.

It is first necessary to find the freezing point of distilled water so as to obtain a standard for comparison. Sufficient distilled water to cover the bulb of the thermometer is poured into the inner tube, which is then placed in position in the outer tube. The water is gently agitated with the stirrer, and the mercury filament sinks rapidly. When the water commences to solidify, the mercury rises rapidly, and then more gradually until it remains steady at a point and then gradually falls again. The highest point to which the mercury rises is the freezing point of the fluid.

In order to obtain accurate results the tube is removed and the water thawed until only a few crystals of ice remain. The process is again carried out, and the freezing point will be found slightly higher, for in ordinary distilled water certain impurities—such as carbonic acid—are present which lower the freezing point. These gases are driven off by the preliminary freezing, and a more accurate result is obtained.

Care must also be exercised that the tubes are perfectly clean, and that no moisture clings to the thermometer bulb when it is changed from one fluid to another.

In similar manner the freezing point of urine is obtained. About 15 to 20 c.c. of the urine are placed in the inner tube. The difference between the freezing point of distilled water and that of the urine represents the lowering of the freezing point.

The urine must be fresh, for ammoniacal decomposition, by changing the urea into ammonium carbonate, brings about a molecular loss which influences the result of the estimation.

1. **Cryoscopy of the urine.**—In studying the freezing point of the urine a point is obtained which is indicated by the sign △, or, to avoid confusion with other fluids, the sign △ U may be used. This represents the molecular concentration of the urine without reference to the nature of the dissolved substances.

In the healthy state the point △ U is liable to considerable variations. Koranyi places it between −1.30 and − 2.20. After copious libations the point may rise to −1° or less; when the urine is concentrated, as after profuse sweating, the figure may be − 2.30 or lower.

Albarran* observed in a neurotic subject with a movable kidney that the point △ U was reduced to −0.46, and Souques and Balthazard have stated that in a case of nervous polyuria the point △ fell to −0.17.

The quantity of urine necessary for examination is from 10 to 18 c.m. If this quantity is not available it is recommended that the fluid be diluted, and the lowered freezing point obtained be multiplied by the figure of dilution. This is, however, fallacious, for according to Koeppe† the dilution produces a dissociation of the salts in solution, so that there is an increase of the molecules, and the estimation of the point △ of the diluted urine will give a figure which is too high.

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* "Exploration des fonctions rénales," 1905.

† *Berl. klin. Woch.*, xxviii., 1901.

In many urines there is precipitation of the salts on cooling. In such urines it is not possible to estimate the molecular concentration accurately by the freezing method, since only the salts that are in solution at freezing point are estimated, and the molecular concentration will be registered at too small a figure. As several authors (Bouchard,* Hamburger,† and Koeppe) have pointed out, there is a deposit of urates at freezing point in a very large number of urines.

Unfortunately, the estimation of the boiling point is no more accurate as a means of estimating the molecular content, for other errors, such as the breaking up of molecules by heat, influence the result.

The quantity of molecules that are precipitated on freezing is a very variable factor, so that no correction can be made which will apply to all urines.

Hamburger dissolved the sediment in hot water, and estimated the freezing point of the solution, and by his calculation the error amounted to 0.051°.

Koeppe estimated the electrical resistance in urines with the urates in solution and after precipitation. The result in three urines was as follows :—

	(I.)	(II.)	(III.)
Urates precipitated at . .	12°	9°	13°
Electrical resistance of urine with urates . . .	270.9	315.6	308.7
Electrical resistance of urine without urates . . .	264.0	309.6	301.4
Difference . . .	6.9	6.0	7.3

Differences in the freezing point which may either increase or diminish the molecular content are also produced by mixing alkaline and acid urines.

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* *Compt. rend. Acad. de Sc.*, cxxviii., p. 64, 1899.

† *Centralbl. f. innere Med.*, xii., 1900.

Zangmeister* has shown that, in order to compare the point Δ of two urines so as to contrast their molecular contents, the fluids must be made of equal volume, and be diluted so that the dissolved salts are held in solution during the freezing.

Considered independently, cryoscopy of the urine is of little value as an indication of the renal function.

The variations in the point Δ U are so considerable, even in the healthy individual, and are dependent upon so many factors—such as the amount of sweat, the quantity of fluid ingested, etc.—that no reliable observations can be made by this method.

2. **Cryoscopy of the urine and estimation of the chlorides (Method of Koranyi).**—Koranyi has advanced a theory of the renal secretion upon which this and several other tests are based.

According to this observer, a solution of sodium chloride filters from the blood into the renal tubules at the glomeruli. As this solution passes down the tubules it undergoes modification. It is concentrated by the absorption of water, and an interchange of molecules between the solution and the blood takes place through the renal cells. Each molecule of sodium chloride which is passed from the urine into the blood is replaced by a molecule of a different nature, such as urea, uric acid, etc., derived from the blood.

According to this theory the number of molecules of chloride of sodium in the urine is of great importance, for if they are increased there has been a reduction of the work done by the renal epithelium in interchanging them for molecules of urea, etc., from the blood, while if they are diminished the urea, etc., should increase, and the renal epithelium has been more active in bringing about the interchanges.

Koranyi, therefore, proposes as a measure of the renal function the relation between the molecular concentration of the urine (that is, the total number of molecules in solution in the urine), and the sodium chloride content (that is, the number of these molecules that are composed of sodium chloride). This is expressed by the formula $\frac{\Delta}{\text{Na Cl.}}$ in which Na Cl. represents the quantity of sodium chloride contained in 100 cubic centimetres of urine. In the normal state this does not exceed 1.7, although in a series of cases it may rise to 2 or over.

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* *Berl. klin. Woch.*, xlix., 1903.

It will be readily understood that this relation depends not upon the renal permeability but upon the rapidity of the secretion, which again corresponds to the activity of the renal circulation.

According to the theory of Koranyi, the more rapidly the urine passes down the tubules the less opportunity will be afforded for the removal of molecules of sodium chloride, and therefore the proportion of sodium chloride in the urine will be greater. Consequently the quotient of $\frac{\Delta}{\text{Na Cl.}}$ will be smaller. On the other hand, a slow circulation through the kidney, as in vascular stasis, will mean a more complete absorption of sodium chloride, and $\frac{\Delta}{\text{Na Cl.}}$ will be increased.

It is necessary to give a diet sufficiently rich in chloride of sodium, for the elimination of sodium chloride at once diminishes when the intake of this salt is reduced, and the $\frac{\Delta}{\text{Na Cl.}}$ will rise if too little sodium chloride is absorbed from the food. But even when such precautions are taken, the conclusions drawn from the Koranyi method are only of value if the renal epithelium is healthy and permits of the interchanges.

3. **Method of Claude and Balthazard.**—This method is based upon the theory of Koranyi, and by it an

attempt is made through a series of formulæ to determine separately the glomerular activity and that of the renal epithelium.

Firstly, however, the formula of Koranyi is corrected in regard to certain fallacies. The point Δ of the urine is corrected for the total volume of urine (V stated in cubic centimetres) for 24 hours, and further the total body weight of the individual is taken into consideration (*P* in kilogrammes). This is expressed in the following formula $\frac{\Delta V}{P}$.

This represents the total molecular content of the urine per kilogramme of body weight, and is termed the "total molecular diuresis" (*diurèse moléculaire totale*) by Claude and Balthazard.

In order to obtain the diuresis of elaborated molecules—that is, the number of molecules of urea, etc.—which have been extracted from the blood in exchange for molecules of sodium chloride, these authors proceed as follows :—

The formula stated above represents the total molecular content of the urine, but since the molecules of sodium chloride which are removed by the renal epithelium are replaced by an equal number of elaborated molecules, the total molecular content will not change, and this formula, therefore, represents the total molecular output of the glomeruli, and expresses the glomerular activity. This varies with the activity of the renal circulation or with diseases of the glomeruli. In order to estimate the work of the renal epithelium, it is necessary to ascertain the number of elaborated molecules (the value δ) contained in the urine. This will be obtained by deducting from Δ of the urine such portion as corresponds to the chloride of sodium.

It is known that an aqueous solution of 1 per cent. of sodium chloride freezes at $-0° 60$. These authors, therefore, "infer that the number of chlorinated molecules will be obtained by multiplying by 60 the quantity of chlorides (p) contained in 100 cubic centimetres of urine. Thus the diuresis of elaborated molecules $\delta = \Delta - (p \times 60)$."*

This may be expressed differently as follows. If from the total molecular content of the urine expressed by the freezing point Δ we subtract the proportion which we believe corresponds to the chloride of sodium molecules $(p \times 60)$, we shall get that proportion of the molecular content which is composed of elaborated molecules (urea, etc.).

Having ascertained the value δ and having corrected it as was done with Δ, the following formula is obtained $\frac{\delta V}{P}$, which expresses the elaborated molecules passed in 24 hours per unit of body weight of the individual.

The following are the normal values of these formulæ :—

(1) Total molecular diuresis $\frac{\Delta V}{P} = 3000$ to 4000.

(2) Diuresis of the elaborated molecules $\frac{\delta V}{P} = 2000$ to 2500.

(3) The sum of the molecular interchange by the renal epithelium $\frac{\Delta}{\delta} = 1.49$ to 1.69.

If δ were taken alone to indicate the activity of the renal epithelium, it would shew variations according to the differences in the composition of the blood.

The activity of the renal epithelium is therefore indicated by the relation of the total molecular content $= \Delta$ to the content of elaborated molecules, $= \delta$.

The following table is given by Claude and Bernard, and is corrected from similar figures in their earlier work†:—

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* "Maladies des reins," Debove, Achard et Castaigne, 1906.

† *Jour. de physiol. et de path. gén.*, 1903, 97.

If	$\frac{\Delta V}{P} =$	6000	then $\frac{\Delta}{\delta}$	does not	exceed	2.20
,,	,,	5500	,,	,,	,,	2.10
,,	,,	5000	,,	,,	,,	2.00
,,	,,	4500	,,	,,	,,	1.90
,,	,,	4000	,,	,,	,,	1.80
,,	,,	3500	,,	,,	,,	1.70
,,	,,	3000	,,	,,	,,	1.60
,,	,,	2500	,,	,,	,,	1.50
,,	,,	2000	,,	,,	,,	1.40
,,	,,	1500	,,	,,	,,	1 30
,,	,,	1000	,,	,,	,,	1.20
,,	,,	500	,,	,,	,,	1.10

A suspicion of deficient renal function will arise when $\frac{\Delta}{\delta}$ is elevated above the value corresponding to $\frac{\Delta\ V}{P}$ in the above table.

The renal inefficiency is "absolute" when the value of $\frac{\Delta\ V}{P}$ and of $\frac{\delta\ V}{P}$ are lowered, although $\frac{\Delta}{\delta}$ may be elevated above what it should be in comparison with $\frac{\Delta\ V}{P}$.

The renal inefficiency is "relative" when the value of $\frac{\Delta\ V}{P}$ and of $\frac{\delta\ V}{P}$ are raised and $\frac{\Delta}{\delta}$ is relatively elevated.

Intermediate types are met with between these two extremes.

According to Claude, "relative renal inefficiency is the expression of a lowered state of the renal function which may be transient. If the type of inefficiency is permanent, one should consider whether a renal lesion, which may be latent and which has produced no clinical signs, does not exist. Finally, it must be remembered that cryoscopy may at times fail to reveal any renal inefficiency in subjects who at the time of examination have a perfect urinary action from the activity of remaining portions of healthy renal tissue, and yet may be the subjects of renal lesions."

A graphic illustration of this method will be found in

Chart 9, which shews a period of temporary renal inefficiency in a case of chronic nephritis.

This method has been severely criticised by Léon Bernard.* This writer points out that the various formulæ of which it consists depend upon the calculation of equivalents, which are frequently open to criticism. The point Δ of the urine is much smaller than it should be, for some part of the dissolved substances are precipitated at the time of freezing. If this is true of the point Δ, the point δ which is calculated from it is also fallacious. The figures V (quantity of urine in 24 hours) and NaCl. (percentage of sodium chloride) are also open to objection, since they are influenced by many conditions, both physiological and pathological, which are quite independent of the renal activity. Finally, the value P (body weight of the individual) is a source of grave error, since it varies so widely in health and disease.

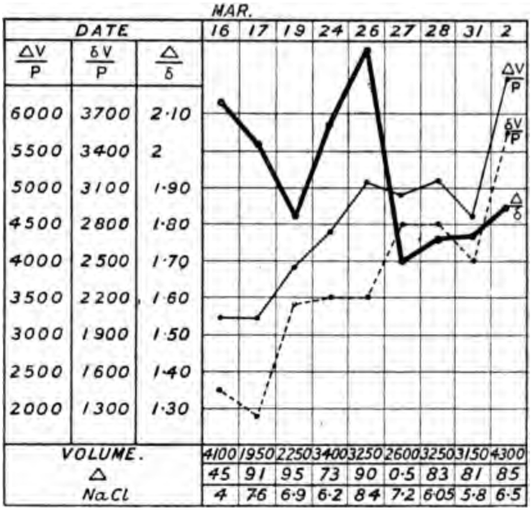

Chart 9.—Chart to illustrate method of Claude and Balthazard.

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* "Les méthodes d'exploration de la perméabilité rénale." Paris, 1904.

The method has also been criticised by Chanoz and Lesiens,* Baraibe† and Brault.‡

4. **Method of Claude and Mauté** § (*La chlorurie alimentaire expérimentale*).—This method consists in the combination of the study of the urine by cryoscopy and an artificially produced alimentary chloruria, or excess of chlorides in the urine.

There is a retention of chlorides in uræmia, in acute nephritis, and in the exacerbations of chronic nephritis, so that sodium chloride given by the mouth only appears in the urine in very small quantities. Achard and Lalper studied this retention of chlorides, and administered for the purpose 10 grains of chloride of sodium. Although in the normal individual the greater part of the salt ingested is passed in the urine in 24 hours, in patients in a state of chloride retention, only a minimal portion was passed in this time.

The application of this method as a test of the renal permeability was due to MM. Claude and Mauté.‖ For this purpose these observers combined the method with that of cryoscopy.

The test is practised as follows. The patient is placed on a rigid milk diet, or at least on a fixed diet poor in chlorides, and a daily examination of the urine is made by the cryoscopic method of Claude and Balthazard. On the second or third day 10 grammes of chloride of sodium in cachet or in solution are added to the food, and this is continued for four days. The examination of the urine is continued during this time until the effects of the ingestion of salt have passed off.

Results of the test.—In healthy individuals there is a slight increase in the quantity of urine and of urea, but the increase in the non-chlorinated substances in the urine does not correspond to the increased quantity of sodium chloride eliminated.

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* *Jour. de phys. et path. gén.*, Sept.–Nov., 1902 and 1903, p. 347.

† Thèse de Lyon, 1901–2.

‡ "Traité de méd. de Bouchard et Brissaud," Vol. v.

§ *Soc. méd. des hôp.*, May 2, 1903.

‖ *Soc. méd. des hôp.*, May, 1902; *Archiv. gén. de méd.*, Aug., 1902; Mauté, Thèse de Paris, Aug., 1903.

In patients suffering from chronic nephritis, the authors were able to distinguish four varieties of reaction.

(1.) In the first variety, which corresponded to a slight degree of nephritis, a trace of artificial renal insufficiency was observed. That is to say, the $\frac{\Delta V}{P}$ and the $\frac{\delta V}{P}$* were separated more widely and the proportion $\frac{\Delta}{\delta}$ increased. These modifications of cryoscopy appeared at the commencement of the administration of chlorides, and disappeared immediately after the test.

(2.) In lesions more advanced there was still an elevation of $\frac{\Delta V}{P}$ caused by the exaggerated elimination of sodium chloride, but the elimination of sodium chloride stimulated the interchange of molecules so that $\frac{\delta V}{P}$ was elevated in a parallel line, and $\frac{\Delta}{\delta}$ was scarcely increased at all. These changes commenced at once with the test and ceased with it.

(3.) In the third variety the renal condition was more advanced. The increase of sodium chloride in the urine did not commence until the day following, or the second day after the first dose, but persisted after the cessation of the test, and might even attain its maximum after the administration of sodium chloride had ceased, in such a manner that the proportion $\frac{\Delta}{\delta}$ did not fall rapidly, and only reached its previous figure on the fourth or fifth day after.

(4.) In the fourth variety the absorption of sodium chloride was not followed by an increase in the urinary chlorides. In addition, cryoscopy shewed no trace of renal inefficiency, but on the contrary, if $\frac{\Delta}{\delta}$ was too much raised (sign of renal inefficiency) before the test, it returned to the normal figure. This was the inverse of the first variety. In place of an artificial renal inefficiency an artificial renal efficiency was obtained.

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* For the explanation of these formulæ, *see* Method of Claude and Bathazard, p. 60.

In all the cases which conformed to this type the nephritis was rapidly fatal.

Examination of the blood.—The estimation of the molecular content of the blood by cryoscopy as a means of estimating the function of the kidneys was introduced into practical medicine by Koranyi.*

The freezing point of the blood is remarkably constant at $-0.56°$, and the point Δ of the serum is practically the same as that of the blood.

The blood may be obtained by bleeding or by means of a cupping glass. If by the latter method, Koranyi recommends that a current of oxygen should be passed through in order to eliminate the carbonic acid which is present.

Koranyi states that where one kidney is inefficient no change is found in the point Δ, but where the function of both kidneys is reduced the point Δ is lowered. A point Δ of $-0.57°$ or $-0.58°$ indicates a reduction in the total renal function. According to Mulon† this margin of reduction is too small, and he considers that Δ $-0.59°$ to $-0.60°$ is necessary before bilateral renal disease may be diagnosed.

From an examination of over 300 cases Kümmel and Rumpel‡ have formulated the following conclusions :—

1. When the kidneys are intact, the molecular concentration of the blood is constant at a point Δ of $-0.56°$.

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* *Monatsber. ü. d. Krankh. d. Harn u. Sex. Org.*, 1889, S. 1 ; *Berl. klin. Woch.*, 1889, S. 97.

† Thèse de Paris, 1900.

‡ *Beitr. zür klin. Chir.*, 1903, Bd. 37, 3 H., S. 788.

2. When there is a bilateral affection of the kidneys there is an increased concentration of the blood, and therefore a lowering of the point △, and a diminished concentration of the urine with a raised point △ U. Kümmel looks upon a point △ of the blood of −0.60° as a contra-indication to nephrectomy. In 16 cases of bilateral renal disease the point △ of the blood was −0.60° to −0.65° C., and in one case it was −0.71°.

3. A unilateral kidney disease does not cause any change in the total renal function as shewn by a raising of the molecular concentration of the blood and a diminished molecular concentration of the urine.

4. When the molecular concentration of the blood is normal there is no interference with the total renal function. In 11 cases in which nephrectomy was performed a freezing point before the operation of −0.56° was taken as a proof of a healthy second kidney. After the operation the remaining organ in all the cases continued to secrete a sufficient quantity of healthy urine, and the freezing point of the blood remained at −0.56°. In one case the freezing point before operation was −0.59° and after the operation −0.57°.

These conclusions have been criticised by Albarran,* who raised the following points :—

(*a*) The lowering of the △ of the blood to −0.60° and beyond may be found apart from lesions of the kidneys.

Kümmel and Rumpel have themselves recognised this fallacy under certain conditions. Thus, in uncompensated cardiac affections, in diabetes, eclampsia, during epileptic attacks, and in the case of a large ovarian cancer, the point △ of the blood was lowered apart from any interference with the renal function. The accumulation of carbonic acid in the blood in respiratory inefficiency, due either to the heart or lungs, may cause lowering of the point △. Koranyi has suggested that a stream of oxygen passed through the blood in such cases would eliminate this error.

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* "Exploration des fonctions rénales," 1905 ; Prem. Congrès de la soc. internat. de Chir., Procès verb., Bruxelles, 1906.

Severe attacks of pain may cause a lowering of the point △ of the blood by influencing the renal circulation. Koranyi has described two such cases. In one the point △ of the blood was −0.76° during an attack of renal colic, and −0.57° after the attack had passed. In a second case, of new growth of the kidney with attacks of colic, the point △ was −0.69° during and − 0.58° after the attack.

This author has also described a case of pyonephrosis which caused interference with circulation of the kidney, so that the point △ was −0.68° before the operation, and after removal of the kidney rose to −0.57°.

Bernard has shewn that chlorosis may cause a lowering of the point △.

(*b*) The normal point △ of the blood (−0.56°) does not shew with certainty that the renal function is efficient.

If for some reason, such as a hydræmic condition of the blood, the point △ is much raised above the normal, the effect of a renal lesion producing insufficient renal activity will be that in lowering the point △ of the blood the figures approach the normal freezing point.

In a case recorded by Israel* there was anuria caused by a left-sided pyonephrosis with disease of the right kidney. In this patient the point △ of the blood was normal (−0.55°).

(*c*) When a single kidney is diseased, the point △ of the blood may be −0.60°. Again, when both kidneys are diseased, the △ of the blood may be normal.

Albarran quotes a case of double calculous pyelonephritis where the following result was obtained :—

△ Blood	−0.56°
△ Urine, left kidney	−1.20°
△ Urine, right kidney	−0.90°

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* *Berl. klin. Woch.*, 1902, No. xxxv.

This author believes that the estimation of the point △ of the blood only possesses a practical interest in exceptional cases. If the point △ of the blood is below −0.58° or −0.60°, it may raise a suspicion of a bilateral lesion, but here the same information may be obtained by collecting the urines of each kidney separately. When it is not possible to study the separated urines of the two kidneys the estimation of the point of the blood is of importance.

In my own cases the method has proved trustworthy, but the number of cases in which I have used it is small.

In cases where the freezing point was depressed, I was able by other means, such as the methylene blue test or phloridzin glycosuria, to confirm the inadequacy of the renal function, or the symptoms were such as to leave no doubt upon the subject.

In a case of enlarged prostate I disregarded a freezing point of the blood −0.66°, as the symptoms of renal inefficiency were insignificant. The patient succumbed to suppression of urine after the operation. In another case, where obstructive anuria was in progress, the point △ of the blood was −0.71°.

Comparative cryoscopy of the urine and blood.—This method was introduced by M. Léon Bernard, and would appear to be an ideal method of estimation of the work of the kidney. By it the molecular contents of the blood and urine are compared.

The freezing point of the normal urine is −1.5° C. to −2° C., and that of the blood serum −0.56°. The quotient of these will be 2.5 to 3.5, and when this figure diminishes we may conclude that there is a diminution of the permeability of the kidney.

These figures are, however, affected in the same way as those of the urine alone.

There is a wide range of variation in the point △ of the urine even in the normal individual and under various conditions which are perfectly physiological.

In this way the quotient of the two estimations may shew a very small figure without there being any impermeability of the kidney. On the other hand, there may be oligurìa with concentrated urine, and the point $\triangle$ may be lowered ($-2°$ or under), when the renal permeability is lowered, and the quotient of the figures is raised so as apparently to indicate a normal renal function.

Bernard has endeavoured to correct this fallacy by taking note of the volume of urine. Thus he multiplies $\frac{\triangle \text{ urine}}{\triangle \text{ serum}}$ by the quantity of urine in cubic centimetres.

The figures thus obtained will vary in the normal individual from 3,000 to 5,000.

There still, however, remains a fallacy. Achard has shewn that there is a remarkable tendency for the composition of the serum to remain fixed, and the $\triangle$ serum therefore varies within the very narrow limits, whatever may be the condition of the kidneys, while the $\triangle$ urine varies very widely under changing conditions.

Bernard himself draws attention to this point in the following words: "The essentially fallacious factor in this method is that the scale of variation of the $\triangle$ serum is very limited, while that of the urine is very extended, which vitiates the comparison of the two figures. This tends in these cases rather to obscure the proper value."

If we test this method on two types of cases—namely, a case of polyuria from interstitial changes in the kidneys, the result of an enlarged prostate, and a case of obstructive oliguria almost amounting to anuria—it will be found that the quotients of these formulæ successfully shew the impaired function when oliguria is present, but fail to demonstrate the gravity of the condition when polyuria is present.

Thus, in the case of polyuria, the formula works out as follows :— $\frac{\Delta U}{\Delta S} \times V = r \quad \frac{-0.47}{-0.66} \times 3070 = 2186$; and in the case of oliguria the figures are :—

$$\frac{\Delta U}{\Delta S} \times V = r \quad \frac{-0.3}{-0.71} \times 60 = 25.35$$

The value of these criticisms is therefore evident.

In spite of these objections, the method from its simplicity has a certain value if it is not measured with mathematical exactitude.

Method of Wright and Kilner.—In order to avoid the use of the considerable quantity of blood which is necessary in estimating the freezing point of the blood, and also with a view to simplifying the examination, Wright and Kilner have introduced the following method.

The principle of the test consists in the observation that at a certain point of dilution of the serum complete destruction (hæmolysis) of the red blood corpuscles takes place, and the same holds good in regard to a solution of red blood corpuscles in the urine. The authors describe their method as follows * :—

A standard quantity of normal red corpuscles suspended in a measured volume of salt solution of a standard strength furnishes a test fluid. The urine—or, as the case may be, the blood fluid (serum) from which that urine is derived—is mixed in progressive dilutions in a capillary tube with measured volumes of the standard suspension of red blood corpuscles. The point is determined at which the urine or serum has been so far diluted as to allow of complete hæmolysis of the standard suspension of red corpuscles.

From these data, taken in association with the data obtained on diluting the suspension of corpuscles with progressive dilutions of a decinormal sodium chloride solution, the concentration of the serum and urine is calculated. The quotient obtained by dividing the latter by the former is denoted "*the excretory quotient.*"

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* *Lancet*, April 2, 1904.

The following procedure is employed in making the suspension of red corpuscles :—

A stout piece of glass tubing, about 2 centimetres in thickness, is taken. It is drawn out in the blowpipe flame into a narrower stem about 5 centimetres in length and 0.5 centimetres thick. The extremity of the stem is again drawn out into a still narrower tube. A graduation mark is now placed with a glass writing pencil upon the stem at a distance of, say, 1.5 centimetres from its extremity. A watery fluid or mercury is now drawn in through the capillary extremity of the tube until the stem is filled in up to the fiduciary mark. Two further graduation marks are now to be added, the points of application of these marks being found by displacing the column of fluid along the capillary stem until its distal limit corresponds in each case to the preceding fiduciary mark. Blood obtained from a prick in the finger is now filled in through the capillary orifice. When the upper limit of the column of blood stands level with the second division mark, the orifice of the tube is introduced into a vessel containing decinormal sodium chloride solution, and the fluid is aspirated into the tube until a 50-fold to 100-fold dilution of the blood has been effected. The extremity of the tube having been sealed, the centrifuge is now brought into use and the centrifugalisation is continued until the corpuscles have all been driven below the upper of the three graduation marks. The supernatant fluid is now pipetted off, and, if necessary, decinormal solution is added until the upper limit of the fluid stands level with the upper graduation mark. The fluid and the red corpuscles are now thoroughly mixed up together. Inasmuch as two volumes of blood furnish one volume of corpuscles, and inasmuch as the plasma has been diluted to practically an unlimited extent, the suspension which has been obtained may without appreciable error be said to correspond to one volume of corpuscles completed to three volumes by decinormal salt solution.

Standardisation of the corpuscles suspension.—When we desire to compare among themselves a number of separate observations on the blood or urine undertaken upon different days, or with the bloods of different persons, it is essential to determine in each how far the standard suspension requires to be diluted before complete hæmolysis is obtained. For this purpose we make a series of progressive dilutions of our decinormal sodium chloride solution. Usually it will suffice if we make a fourfold, fivefold, and sixfold and intermediate dilution. We now take up into our capillary pipette one volume of each of these dilutions, mixing in each case one volume of the suspension of corpuscles. Holding at arm's length the capillary pipette which contains the series of mixtures, and disposing the tube so that light may strike upon it obliquely, we take cognisance of the hæmolytic effect. Opacity and a bright appearance, referable to the reflection of light to the eye, indicate incomplete transparency, and a dark colouration due to the absence of reflection indicates complete hæmolysis. Usually complete hæmolysis is obtained on using one volume of the $\frac{N}{50}$ (0.117 per cent.) or $\frac{N}{60}$ (circ. 0.1 per cent.) sodium chloride solution with one volume of the corpuscular suspension.

The technique for making the progressive dilution of serum, or, as the case may be, of the urine, and for mixing these in each case with equal volumes of the standardised suspension of red corpuscles, is the same as that employed in the standardisation of the corpuscular suspension. It is convenient in each case to begin with a four-fold dilution and then to follow on with an eight-fold, sixteen-fold, and, if necessary, thirty-two-fold dilution. When a dilution which gives complete hæmolysis is arrived at, we can, by going back upon the original four-fold dilution, make for ourselves the particular intermediate dilution which may be required.

Usually, in the case of the normal serum, complete hæmolysis will be achieved with the eight-fold, but not with the six-fold dilution. In the case of the normal urine, it will be achieved with either the 16, 24, or 32-fold dilution.

We obtain a convenient—but only approximately accurate—expression for the concentration of the serum or urine we are testing by setting it down as *x*-times greater than that of the salt solution which was, in the standardisation of the corpuscular suspension, found to affect complete hæmolysis, *x* representing in this expression the dilution of the serum or urine which had been arrived at when the complete hæmolytic effect was obtained.

ELECTRICAL RESISTANCE OF THE URINE AND THE BLOOD

I.—ELECTRICAL RESISTANCE OF THE URINE

The conductivity of a substance to electricity is the inverse of its resistance, and the conductivity may be expressed in terms of resistance. The unit of resistance is called an ohm. Aqueous solutions are known to offer a variable resistance to the passage of an electrical current according to their composition.

In 1891, before the Royal Society of Edinburgh, Dr. Dawson Turner* gave an account of experiments he had made to ascertain and compare the electrical resistance of various kinds of urine both in health and disease. To avoid polarisation, the measurements were made by means of a Wheatstone's bridge with alternating currents and a telephone, and at a temperature of 65° F.

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* *Edin. Med. Jour.*, April, 1907.

Later Bordier, of Lyons,* studied the electrical resistance of healthy and diseased urines.

The *specific resistance* of a urine is the resistance offered by a thickness of one centimetre and a section of one centimetre square of the fluid.

The urine owes its conductivity almost entirely to its mineral components, and not at all to its organic contents.

If the total conductivity of the urine be subtracted from the conductivity of a solution of chloride of sodium of the same concentration, the difference corresponds to the other mineral salts in the urine, such as the phosphates and sulphates.

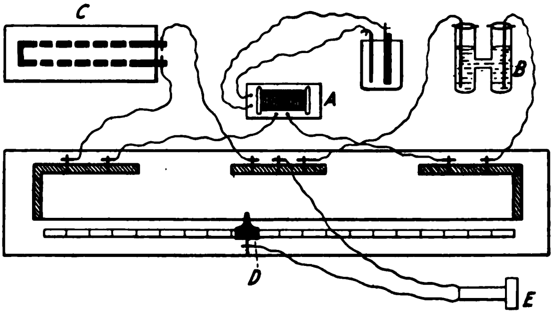

Fig. 3.—Apparatus for measuring electrical conductivity of urine.

A, induction coil; B, vessel containing fluid; C, rheostat; D, movable contact; E, telephone.

The resistance of urine is very small.

The proportion $\frac{P}{P\,1} = \frac{\text{resistance of urine}}{\text{resistance of Na Cl. solution}}$ should be less than 1; normally it is 0.7.

A constant current is unsuited for the measurement of the resistance of solutions on account of polarisation. Kohlrausch uses an alternating current, in which the polarisation is reduced to a minimum.

The apparatus of Kohlrausch (Fig. 3) is arranged on the principle of a Wheatstone bridge, the fluid to be measured being interposed on the one side of the galvanometer and a resistance coil on the other. A telephone is used instead of a galvanometer. The fluid is placed in a specially constructed vessel and the induction current started. The resistance is increased until the singing of the induction current can no longer be heard in the telephone.

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* Quoted by Debove, Achard et Castaigne, "Maladies des Reins," 1906.

Dr. Dawson Turner,* in discussing his observations on urines in healthy and diseased individuals, states "that the specific resistance of a normal urine amounts to about 45 ohms,† and that it varies, as a rule, inversely with the specific gravity. The latter is a measure of the amount of solids in solution, and particularly of the urea. It might be supposed, then, that the resistance depends also mainly upon the amount of urea; this, however, is not the case." "It is clearly apparent that the electrical resistance depends almost wholly upon the salts, chlorides, phosphates, sulphates, etc., and that it is only when these are absent or diminished that the influence of the urea makes itself felt. The resistance is therefore a measure of the chemically active substance in a urine, of the salts, and to a very much less degree of the inert urea."

In a normal urine the resistance and the specific gravity are in inverse proportion. In acute croupous pneumonia, however, the electrical resistance is much higher than would be expected from the specific gravity of the urine, and this is to be referred to the great diminution of chlorides in the urine in this disease. It is more difficult to explain the increased resistance in a diabetic urine, when both the resistance and the specific gravity are greatly increased, for the addition of sugar lowers the resistance of distilled water. According to Turner, the sugar "does to a slight extent raise the resistance of a saline solution," probably by hindering diffusion by its viscosity. The increased resistance depends, however, almost wholly upon the relative diminution in the salts in the urine in diabetes.

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* "Practical Medical Electricity," 1902.

† 42.5 ohms in a later article, *Edin. Med. Jour.*, April, 1902.

In acute and chronic Bright's disease, mitral disease and anæmia the resistance is high. It is increased by taking copious draughts of water and diminished by the injection of salt.

The following data are selected from Dr. Dawson Turner's tables :—

Condition.	*Specific gravity.*	*Reaction.*	*Urea grains per oz.*	*Albumin.*	*Sugar grains per oz.*	*Specific resistance. Ohms.*
Normal . .	1027	Acid	13.1	0	0	38 to 59 (Average 45).
Diabetes .	1034	Acid	4.68	0	25	156.4
Sub-acute Bright's Disease .	1011	Acid	4	albumin	0	114.75
Pernicious Anæmia .	1014	Acid	7.72	0	0	115.6

2.—ELECTRICAL RESISTANCE OF BLOOD AND URINE

The same author has endeavoured to estimate the electrical resistance of the blood. The principal difficulty depends upon the fact that only very small quantities of blood can be obtained at one time. The best and most recent results were obtained by placing 5 c.mm. of freshly drawn blood between two cup-shaped electrodes 3 mm. in diameter, coated with spongy platinum and fixed at 2 mm. apart.

By making the observations before coagulation or evaporation could occur, fairly constant results were obtained.

Wilson* has shewn that the resistance of serum from clotted blood is the same as that of the corresponding plasma, and that unclotted blood and defibrinated blood have the same resistance.

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* *Amer. Jour. of Physiol.*, March, 1905.

The specific resistance of the blood according to Dawson Turner is about 150 ohms, and the resistance depends upon the salt concentration and the relative volume of the corpuscles to the serum. Changes in these two factors produce opposite effects—the greater the salt concentration the lower the resistance, and the greater the number of red cells present the higher the resistance. "A blood of high resistance indicates that the proportion of salts in the blood is small, or that the proportion of corpuscles present is large. Hence a high resistance of the blood but a low resistance of the urine is indicative of health." A ratio of the electrical resistance of the blood and urine was suggested under the name of the "hæmorenal salt index."

In health this was equal to 3, 4, or 5 whole numbers, thus $\frac{900}{225} = 4$. The higher this number, the healthier—other things being equal—is the condition of the patient. Any index below 3 is abnormal and suspicious, and an index below 2 is serious. Surgical interference with kidney lesions is contra-indicated if the index is much below 3.

SURFACE TENSION OF URINE

It is known that under certain pathological conditions the surface tension of the urine is liable to considerable disturbance. Although at present, from the paucity of observations in different diseases, the value of this method of examination of the urine cannot even be surmised, the results obtained by Drs. W. D. and F. G. Donnan suggest that it may find a sphere of usefulness in the future. I shall therefore quote freely from an investigation* carried out by these observers. The surface tension of a fluid is readily measured by allowing it to drop slowly from a pipette and counting the number of drops contained in a given volume. The following apparatus is suggested by Drs. Donnan for clinical use (Fig. 4). A dropping pipette is provided in its upper stem with a tap. The lower stem of the pipette passes through the rubber stopper, which closes the upper end of a glass cylinder. The latter is held firmly in the neck of a water jacket by means of a rubber stopper. The temperature of the liquid at the point where the drops detach themselves is as nearly as possible the same as that of the fluid in the water jacket which is kept at the desired figure. It is necessary that the drops should form slowly, and that the total time of outflow should vary as little as possible. This is effected by allowing the air which replaces the liquid in the pipette to pass through a very narrow capillary tube provided with a wider piece of tubing, which contains cotton wool and filters the air passing through. In making a determination the dropping tube is filled with the urine, and by means of the handle is thrust up into the neck of the jacket, so that the orifice of the pipette is plunged well under the liquid in the tube. The taps being open, the pipette is filled some distance above the water mark by suction applied to the end of the rubber tubing. The taps are then closed. After the liquid in

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* *Brit. Med. Jour.*, Dec. 23, 1905.

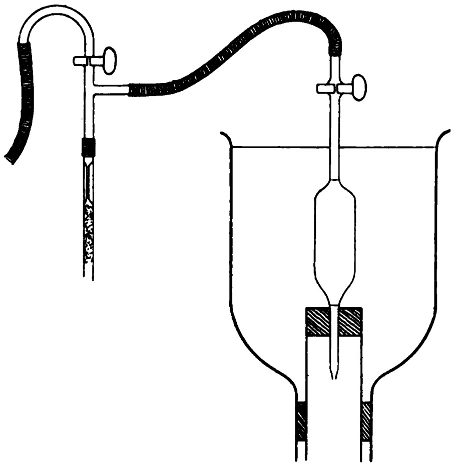

Fig. 4.—Donnan apparatus for measuring the surface tension of urine.

the pipette has been given time to rise to the temperature of the water jacket the outlet tap is opened, and counting begun as soon as the level of the liquid arrives at the upper mark on the stem of the pipette.

A variation in temperature amounting to one degree produces a scarcely perceptible effect on the drop number. In all cases the surface tension is given as a percentage of that of pure water at 16° C., which has a drop number of 199. Thus, in the case of a urine giving a drop number of 225 and a density of 1021, we have surface tension $\frac{199}{225} \times 1021 \times 100 = 90.3$ per cent. "If we take as the surface tension of pure water at 16° C. the value 75 (dynes per cm.), it is only necessary to multiply the percentage numbers given by 0.75 to convert them to surface tensions in dynes per cm."

The surface tension of the urine of healthy individuals is subject to considerable fluctuations. A high surface tension is associated with a comparatively low density, while in certain cases where normal urine shews a low surface tension this is usually associated with a relatively high density. In considering the surface tension of a sample of urine the density must also be noted as an index of the general degree of concentration of the urinary constituents.

Morning urines are uniformly characterised by a high density and a low surface tension. Unusual exertion causes a great fall in the surface tension, which is accompanied by a rise in density corresponding to the concentration of the urine. A high density is not necessarily associated with a low surface tension. It is not known what constituents cause the surface tension of normal urine to be 10 per cent. lower than that of water. The difference is not due to any of the inorganic salts, since these are known to increase the surface tension of water. Again, experiments on the concentration of urea and urates shew that these bodies have practically no effect. Soaps, bile acids, and the higher aliphatic alcohols and acids are known to possess the property of lowering the surface tension of water to a marked degree.

Until we know the exact nature of the effective substances and their origin it will be difficult to interpret the variation of surface tension observed under apparently normal conditions in the urine. This uncertainty diminishes the value of surface tension observations as an aid to diagnosis in pathological conditions with the exception of jaundice, where a definite connection between the surface tension of the urine and the presence of certain pathological constituents has been established.

Drs. Donnan made a series of observations on the surface tension of normal urine to which various substances had been added.

The following figures are taken from their tables :—

Substance added.	*Per cent.*	*Density.*	*Drop number.*	*Surface tension.*
Dextrose	10.0	1066	233½	90.8
Sodium taurocholate .	0.0825	1026	312½	65.3
Sodium glycocholate .	0.0664	1022	326	62.4
Acetose	1.0	1021	230	88.3
Albumin	?	1024	221	92.4

The surface tension of urine under pathological conditions was also examined in a few cases.

Disease.	*Per cent.*	*Density.*	*Drop number.*	*Surface tension.*
Diabetes mellitus . .	4	1030	226	90.7
Gouty glycosuria . .	5.2	1027	217	94.2
Albuminuria . . .	—	1020	248	81.8
Pernicious anæmia . .	—	1016	231	87.5

CHAPTER IV

ELIMINATION OF CERTAIN SUBSTANCES BY THE KIDNEYS

Historical—Evolution of Tests Based upon the Elimination of Certain Substances by the Kidneys—Methylene Blue Test—Technique of Methylene Blue Test—Condition of the Blood and Urine during the Test

It has long been recognised that the elimination of certain substances which pass out through the kidneys is hindered by diseases of these organs. In 1820 Hahn observed that the odour of violets, which normally scents the urine after the ingestion of turpentine, failed in a gouty subject. Later (1837) Rayer noted that asparagus did not produce the characteristic odour of the urine in cases of Bright's disease. These observations were confirmed by Corlieu in 1856 and Bauvais in 1858.

The modified excretion of certain drugs in the urine, and the danger of their retention in the system in renal diseases, led to a series of observations by Todd (1857) in regard to Dover's powder, Charcot and Cornil (1864) on opium, and Roberts (1865) on mercury. Duckworth made a methodical investigation into the elimination of iodides, alkaline carbonates, salts of potassium, and soda, and shewed that there was a delay in the appearance of these substances in the urine in Bright's disease. Chauvet (1877) noted the same delay in the elimination of sulphate of quinine, bromide of potassium, mercury, and salicylic acid, and he further demonstrated a reduction in the quantity of the substance eliminated.

Bouchard, in the same year, suggested that observations might be made upon the urinary secretion by the administration of fuchsin. These investigations were followed by the theses of Bruneau (Paris, 1880) and Vincent, and the work of Desprez on the elimination of iodides, and of Mlle. Chopin (1889) on salicylic acid. The last-named observer shewed that in Bright's disease this drug commenced to pass later, had a longer period of elimination, and that the total quantity eliminated was reduced. Gastinal (1888), Bourdette, Lafay (1893), and Noel successively wrote upon the subject. Finally Achard and Castaigne proposed* the injection of methylene blue and the observation of variations in the elimination of this dye in the urine as a means of estimating the permeability of the kidneys.

In 1898 Chauffard and Cavasse shewed that variations in elimination of this substance were found in abnormal conditions of the liver.

In the same year Guyon and Albarran studied the elimination of methylene blue after catheterisation of the ureters. Professor Lepine† used a red colouring material, rosaniline trisulphate of soda, and Dreyfus‡ further developed this test. Since that date much has been written on the different tests by Nesti,§ Müller,¶ Vidal,‖ Blonard,** Bard and Bonnet,†† and others.

METHYLENE BLUE TEST

If methylene blue be administered in the form of pill by the mouth, or injected in solution into the muscles, the urine, after a varying time, assumes a green or blue colour. This colouration of the urine continues from one to several days, and then gradually passes off.

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* *Soc. méd. des hôp.*, April, 1893.
† *Lyon méd.*, Feb. 20, 1898.
‡ Thèse de Lyon, 1898.
§ *La Sentimenta Med.*, July, 1898.
¶ *Wien. klin. Woch.*, June, 1899.
‖ *Soc. méd. des hôp.*, Feb., 1900.
** Thèse de Paris, 1900.
†† *Archiv. gén. de méd.*, Feb., 1898.

Methylene blue is an aniline derivative (tetramethylthionine chloride), which is readily soluble in water. The methylene blue should be pure, free from arsenic which may be present in the article of commerce. It is necessary to make certain that some other form of blue is not supplied. During the course of my observations in this test I had the misfortune to use a blue in 16 cases of urinary disease which produced no blue colouration in the urine; nor was the dye excreted in the form of any of the known colourless derivatives of methylene blue. The patients suffered from some degree of malaise and the urine took a deep orange pink colour.

The methylene blue should be without particles or thickness, and should dissolve completely in water without the addition of alcohol. On spectroscopic examination of a solution of methylene blue a very dark band appears in the red between B and C, and in more concentrated solutions a lighter band in the orange between C and D. These serve to distinguish methylene blue from some other aniline blues.

According to Underhill and Closson,* methylene blue is a mixture of methylene blue and methylene azure, and it is impossible to obtain methylene blue entirely free from methylene azure.

The administration of methylene blue by the mouth introduces an element of uncertainty from the varying rate and completeness of absorption, so that this method is untrustworthy when compared with that of intramuscular injection.

The blue is absorbed into the circulation from the place of injection in the form of a colourless derivative. This reduction of methylene blue takes place only in living tissues. The colourless derivative or chromogen is transformed into methylene blue in the liver and kidneys, and excreted in the bile and urine. The blue excreted by the liver is apparently reabsorbed into the circulation from the intestine.

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* *Amer. Jour. of Phys.*, 1905, xiii., 358.

Methylene blue is excreted in the urine in two forms, partly as methylene blue and partly as a colourless derivative or chromogen. By boiling the urine containing the chromogen, a part of it is transformed into blue, and if acetic acid be added the remaining part of the chromogen becomes coloured. The addition of hydrochloric acid, peroxide of hydrogen, or potassium acid phosphate will bring about the same result.

The whole amount of methylene blue which is injected is not excreted by the kidneys either as blue or as chromogen. That excreted in the bile is reabsorbed, so that the loss is not to be accounted for in this way. According to Achard, about 50 per cent. of the blue injected is found in the urine during the first twenty-four hours in a healthy subject.

Limossier and Lemoine* have shewn that the position of the individual exercises a considerable influence on the elimination of methylene blue. These observers state that the quantity eliminated in a given space of time may be greater by four or five times if the patient is lying in bed than if he is going about.

Technique of the methylene blue test.—The greater accuracy of dosage and certainty of absorption render the intramuscular method of administration preferable to that in the form of pill by the mouth.

A dose of ½ grain may be given in pill form, and the dosage in all cases should be the same.

The intramuscular injections are made into the buttock. After cleansing the skin, 15 minims of a 5 per cent. aqueous solution of methylene blue are slowly injected into the muscles of the buttock. Some degree of pain was caused by the injection in nearly all my cases, but this usually passed off in about an hour. No other local reaction was observed.

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* *Gaz. méd. des hôp.*, March, May, 1903.

The patient is directed to pass water at the time of the injection. The urine is collected 15 minutes later, by catheter if necessary, and again at the end of half an hour after the injection, then one hour, two hours, or every hour until the blue or green tint has become fairly established in the urine. The whole of the coloured urine passed is collected, and a sample of each 24 hours' specimen is set aside for examination. The colour of the specimens and variations in the depth of the staining are specially noted. A sample of the first clear urine after the disappearance of the blue is preserved. Each sample is examined for methylene blue against a white background.

Where no change of colour has occurred the testing for chromogen may at once be proceeded with. A few drops of acetic acid are added to the urine, and this is then boiled.

The change takes place best when the acid is present in fair quantity. Peroxide of hydrogen may be substituted for the acid, but does not act so rapidly or so powerfully. About five minutes' boiling is sometimes necessary before the change in colour is complete. If the urine is already tinted with blue, the colouring matter is extracted by shaking in a test tube with chloroform (or nitrobenzine) and allowing the chloroform to settle at the bottom of the tube. The clear urine is then decanted and boiled with acid to demonstrate the chromogen. Several extractions with chloroform may be necessary before the whole of the blue is removed.

The clear urine before the appearance of blue, and that after its disappearance, should be tested for chromogen as well as each specimen during the elimination of the blue.

In a healthy individual, leading an ordinary life without excessive exercise or manual labour, who does not drink large quantities of fluid during the test, the following may be looked upon as a typical course after the injection of 15 minims of methylene blue into the buttock.

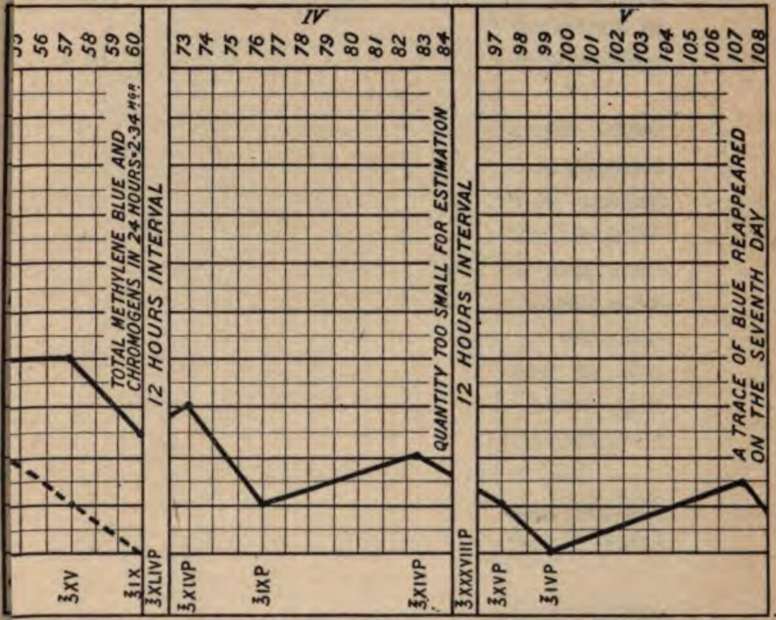
In the first urine drawn (15 minutes), there is no trace of methylene blue, but on testing with heat and acetic acid chromogen may be detected. This is not invariably the case, but in all my observations on healthy individuals the excretion of chromogen commenced before methylene blue could be detected in the urine. Sometimes five minutes, at other times a period of fifteen minutes, elapsed before the methylene blue tinged the urine after chromogen had been detected.

Blue colouration of the urine occurs about half an hour after the injection, and will usually be detected in the second sample of urine. It rapidly becomes more and more intense. The first appearance may be only a slight darkening of the urine, the next is a greenish tint, and then an olive green or a bright emerald green, then a bluish green, prussian blue, and finally a deep blue colour. The colour may not, however, pass beyond an emerald green.

During the earlier part of the elimination chromogen is present in greater quantity than methylene blue. This preponderance of chromogen may be maintained for the first four or five hours, when the methylene blue gradually gains the ascendency which it maintains during the remainder of the elimination. The excretion of chromogen usually ceases some hours before the last traces of methylene blue disappear. The excretion of blue continues for 40 to 60 hours, sometimes it is over sooner than this, nothing remaining after 36 hours. It may be prolonged beyond 60 hours in health, and on occasion may recur after having apparently disappeared. During the elimination of the blue, a draught of fluid will produce a very appreciable fading of the colour, not only of the blue but of the chromogen, and this may extend over an hour or even more.

In studying the elimination of methylene blue in health and disease, there are several points which claim attention :—

1. The commencement of elimination.
2. The duration.
3. The quantity of colouring material eliminated as



ine, chromogen by dotted line. The Chart shews the total daily elimination
elimination was prolonged as traces beyond the normal duration.

An early onset of elimination has been observed by Bard† in parenchymatous nephritis. In this form of nephritis the blue usually appears before the first half-hour.

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* Albarran, "Exploration des fonctions rénales," 1905.

† *Gaz. hébdom.*, May 27, 1897, p. 494.

1. The commencement of elimination.
2. The duration.
3. The quantity of colouring material eliminated as blue and as chromogen.
4. Variations and irregularities in the course of elimination.

1. **The commencement of elimination.**—In health the urine shews a faint bluish tinge half an hour after the injection of methylene blue, and this rapidly increases in intensity, so that at the end of the first hour the urine is fairly coloured with blue (Chart 10).

Before the first trace of blue appears the test for chromogen shews that the colourless derivative of methylene blue is already passing out in the urine. It is usually possible to detect the presence of chromogen in the urine passed a quarter of an hour after the injection, and, even if this is not so, the first urine which is faintly tinged with methylene blue will give a strongly marked blue with the chromogen test. This relation of the chromogen to the methylene blue in the urine is the rule both in health and in disease. Further, where delay occurs in the excretion of the blue the chromogen excretion is likewise delayed.

In pathological conditions of the kidney the excretion of blue is delayed. It may occur after one, two, or even three or more hours (Chart 13).

Albarran and Bernard* have recorded cases in which very considerable delay in the commencement of excretion was observed, yet the renal lesion was of quite insignificant character. In two cases of movable kidney the blue appeared 2½ and 3½ hours after the injection respectively.

An early onset of elimination has been observed by Bard† in parenchymatous nephritis. In this form of nephritis the blue usually appears before the first half-hour.

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* Albarran, "Exploration des fonctions rénales," 1905.
† *Gaz. hébdom.*, May 27, 1897, p. 494.

In one of Jouffray's* cases of parenchymatous nephritis, this rapid elimination of blue was observed.

2. **Duration of elimination.**—In a healthy subject the whole excretion of blue is said to be completed in 35 to 60 hours. My own observations seem to shew that this period is too short. After the first wave of elimination had passed, traces were observed in the urine during the fourth, fifth, and even in the sixth or seventh days in some healthy individuals (Charts 11 and 12).

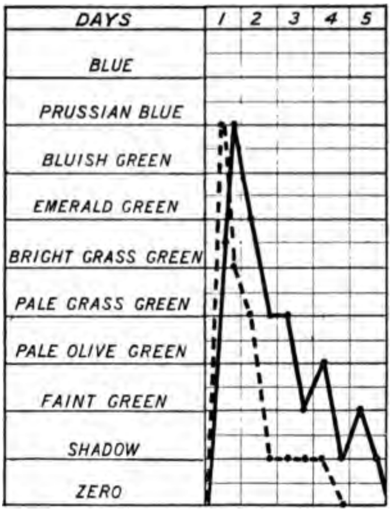

Chart 11.—Elimination of methylene blue in healthy subject prolonged to fifth day. Blue shewn by continuous line, chromogen by dotted line.

In pathological conditions of the kidney the excretion may take place within these limits, but some change is usually observed in the duration of excretion.

The excretion in these cases may be shortened or prolonged.

Shortened elimination.—This may result from the rapid passage of excessive quantity of methylene blue in the urine, and, according to Bard, represents an excessive permeability found in cases of parenchymatous nephritis. In Jouffray's case the elimination was over in 19 hours.

On the other hand, the shortened elimination may coincide with a marked lowering of the permeability of the kidneys, and the quantity of the blue excreted is very small.

Achard and Castaigne† explain this phenomenon in the following manner :—In the case of a diseased kidney with a lowered permeability a very high proportion of methylene blue must be present in the blood in order to allow a small quantity of blue to pass away. This takes place usually at the period which corresponds in the normal course with the maximum elimination. When the quantity of blue in the blood falls the kidney does not allow any to pass, or only a very small quantity, too small to be detected by our means of observation.

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* Thèse de Lyon, 1903.

† *Bull. et Mem. de la Soc. méd. des hôp.*, Feb. 24, 1899.

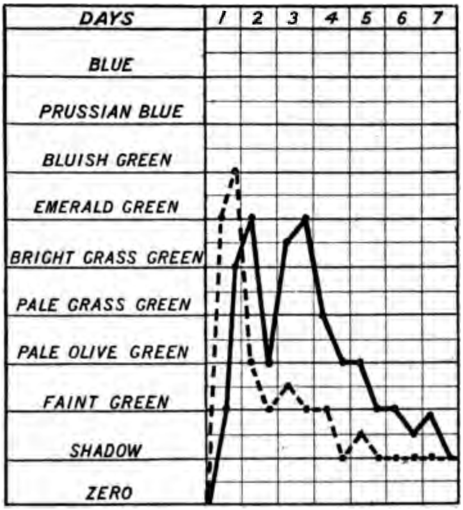

Chart 12.—Elimination of methylene blue in healthy subject prolonged to seventh day. Blue shewn by continuous line, chromogen by dotted line.

It appears to me much more likely that in cases where the diseased kidneys do not eliminate blue but pass chromogen, the difficulty lies in the transformation of chromogen into blue, and that the diseased kidneys lack this power.

Prolonged elimination.—The period of time during which the methylene blue is present in the urine varies with the renal permeability. Where a certain portion of the renal tissue is destroyed, the remaining healthy tissue is unable to eliminate the dye as rapidly as when the normal amount of kidney tissue is actively at work.

This variation has been observed especially in cases of interstitial nephritis when traces of methylene blue may persist in the urine for 6 or even 10 days, and very rarely as long as 15 days after the injection.

Prolongation of elimination is also met with in surgical disorders of the kidneys. I have observed the excretion of blue during a period of 8 days and 17 hours in a man of 67 years who suffered from enlarged prostate and interstitial changes in the kidneys resulting therefrom. He was also the subject of chronic bronchitis and emphysema (Chart 13).

Several types of prolongation have been recognised. In a slight degree of impermeability the duration of elimination may remain normal, but faint traces of blue may be detected in the urine for several days after the main wave of excretion is past. Again, the excretion of appreciable quantities of blue may continue during several days beyond the normal time, but the total quantity which is eliminated does not differ greatly from the normal. More frequently the prolonged elimination co-exists with a diminution in the quantity eliminated. After the first twenty-four hours mere traces of the blue are passed during a prolonged period.

3. **The quantity of methylene blue eliminated.**—Several methods have been used to estimate the quantity of blue eliminated. For the purposes of quantitative estimation the chromogen must be transformed into blue, so that the total output is reckoned.

All the methods are colorimetric, and are therefore open to some degree of fallacy. The comparison of the coloured urine with a solution of methylene blue of measured strength is the means by which the estimation is made. A fallacy is introduced by the yellow colour of the urine, and it is necessary that the solution with which the blue urine is compared should have the same yellow tint. This may be obtained by adding a known quantity of blue to a sample of the patient's own urine, taken before the blue commences to pass, or the requisite colour may be obtained by the addition of potassium bichromate solution.

The most accurate method is that described by Achard and Clerc.* Two similar beakers are used. In the one are placed 25 cubic centimetres of the blue urine which has previously been boiled with acetic acid, in the other are placed 25 cubic centimetres of the mixed urine of 24 hours before the commencement of the test. To each of these is added a like quantity of water until the blue urine is reduced to a pale tint. Usually about two or three litres of water are required.

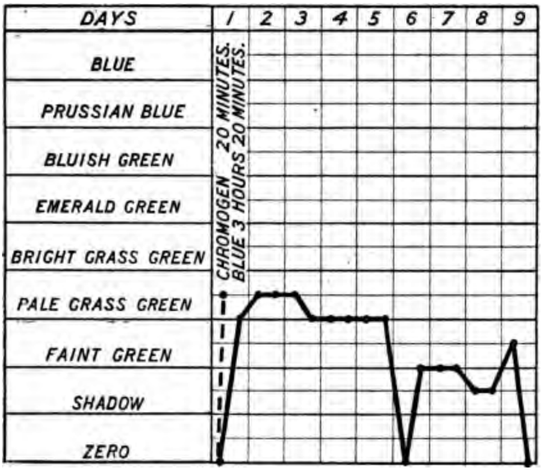

Chart 13.—Enlarged prostate, interstitial nephritis. Delayed, prolonged, and diminished elimination of methylene blue with single intermission on sixth day.

To the second beaker a weak solution of methylene blue (1 in 10,000) is added from a graduated burette drop by drop with constant stirring.

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* *Bull. et Mém. de la Soc. méd. des hôp.*, 1900, p. 96.

When the tint of the two beakers is exactly similar, the quantity of the methylene blue solution which has been used is noted.

This quantity exactly represents the colouring material contained in 25 cubic centimetres of the urine collected during 24 hours after the injection. From this, the amount passed in the total urine of the 24 hours is readily calculated. Thus, if 3.3 c.c. of the titrated solution of blue (1 in 10,000), which represents 0.33 milligrammes of blue, have been added to the uncoloured urine, this indicates the quantity of blue contained in 25 c.c. of coloured urine. If the total quantity of urine passed during the 24 hours following the injection is 2,130 c.c. the total quantity of blue in this will be :—

$$\frac{0.33 \text{ mgr.} \times 2130}{25} = 28.11 \text{ mgr.}$$

In the healthy state the total quantity of blue eliminated in the first 24 hours is a fraction of the total injection, usually about 25 to 30 milligrammes.

It is not, however, necessary to estimate the total quantity with such accuracy where it is merely desired to obtain an indication as to the diminution of the renal permeability.

In making accurate observations upon the hourly excretion of methylene blue, small quantities of blue urine will be examined, and the comparative test may be made in test tubes. I have used the apparatus illustrated in Fig. 5.

A dilution of the standard solution of methylene blue to 1 in 10,000 gives a very pale blue, and it will be found more convenient to work with a solution of 1 in 5,000.

When the chromogen and blue are estimated separately, as may readily be done, it will be found that a chromogen blue urine of apparently similar depth of colour to a methylene blue urine will require a considerably greater quantity of standard solution to produce an equal shade.

For the purpose of obtaining records for comparison of various cases, charts were constructed in which some attempt was made to describe the varying tints assumed by the methylene blue urine.

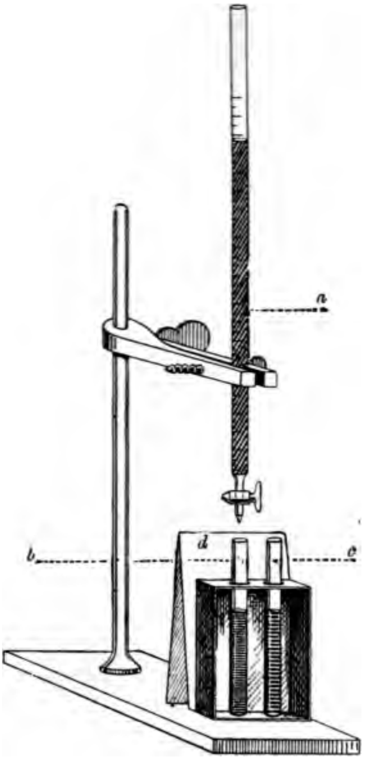

Fig. 5.—Apparatus used for quantitative estimation of methylene blue in urine.

a, burette containing solution of methylene blue of known strength ; *b*, sample of patient's urine passed before injection of blue, and into which blue solution is now dropped; *c*, sample of urine containing eliminated methylene blue ; *d*, sheet of white paper.

This method was found sufficiently reliable for the comparison of different cases.

Variations in the colouration of the urine occur in the elimination of blue by the healthy kidneys. The temporary polyuria produced by tea or a large draught of water reduces the percentage of colouring material in the urine for an hour or more (Chart 14).

In some subjects, without any detectable renal disease, the depth of colouring of the urine does not at any time exceed a grass green ; in others the colour is a deep blue. In order that the total quantity of blue eliminated may be estimated, the duration of the excretion must be reckoned in addition to the intensity of colouring.

The total quantity of blue is diminished in interstitial nephritis, and this is shewn by the pale colour of the urine containing blue during the first 24 hours. In parenchymatous nephritis, on the other hand, the colour may be intense, and at the same time the duration of the elimination is short.

It may happen that no blue is excreted, and this is usually a sign of the gravest forms of renal lesion of the sclerotic type.

On the other hand, it has occurred that, in a patient with no appreciable renal lesion, methylene blue has failed to appear in the urine. The following case may be cited in illustration, although, as the blue was given by the mouth, it is open to the objection that the dye may never have been absorbed.

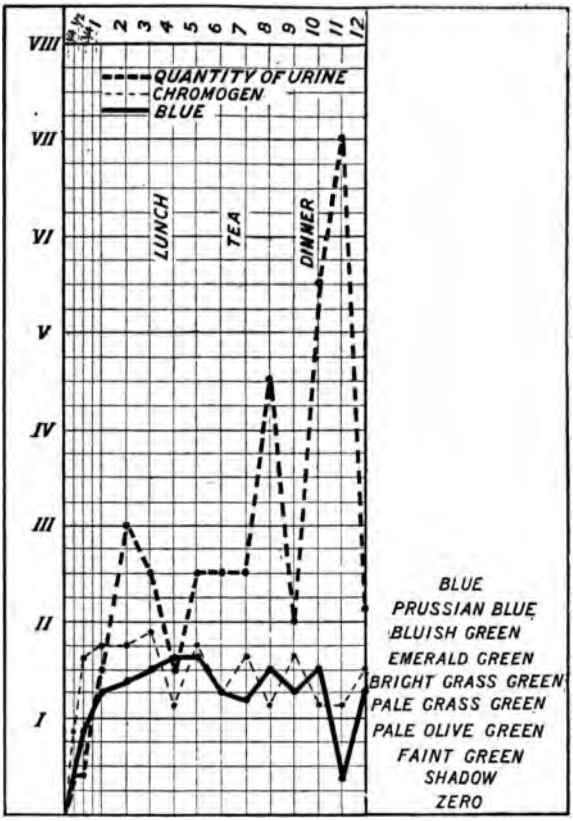

Chart 14.—Normal elimination of methylene blue (continuous line) and chromogen (fine dotted line) compared with quantity of urine (heavy dotted line) during first twenty-four hours after injection.

The patient was a young man (C. S. P.) of 24 years, who was the subject of bilharzia cystitis. He had bathed in the Vaal river in South Africa, and his vesical symptoms commenced six months later. His urine contained a normal percentage of urea, and albumin was only present in the periods during which he suffered from slight terminal hæmaturia. There were no signs of renal disease. He took half a grain of methylene blue in pill daily for a month, and this was later increased to two grains. The methylene blue was given for its therapeutic action, and was continued during three months. At no time was there any trace of blue or chromogen in his urine. The fæces were sometimes stained with blue, but more often not.

Pugnat and Revilliod have noted two cases of chronic nephritis, one of acute parenchymatous nephritis and one of mitral insufficiency with œdema, where neither methylene blue nor chromogen appeared in the urine.

4. **The course of elimination.**—By collecting and comparing the urine at short intervals during the elimination of methylene blue it will be found that the most common course of elimination is a rapid increase to a maximum intensity of colour, followed by a more gradual but regular fall until the blue has disappeared from the urine. The excretion usually reaches its highest point 3 hours after the injection and remains at this level for 4 or 5 hours.

It may, however, happen that the elimination of blue falls and then rises again, or it may fall and completely disappear and later recommence (Chart 15).

According to Chauffard, Cavasse, and Castaigne,* these disturbances of the rhythm of elimination occur in affections of the liver, and are characteristic of hepatic inefficiency.

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* Chauffard, *Presse méd.*, Jan. 8, 1898, p. 13.
Chauffard et Cavasse, *Presse méd.*, March 12, 1898, p. 129.
Chauffard et Castaigne, *Bull. et Mém. de la Soc. méd. des hôp.*, April 22, 1898, p. 359.
Oulmont et Ramond, *Presse méd.*, April 29, 1899, p. 201.
Ménétrier, *Bull. et Mém. de la Soc. méd. des hôp.*, June 22, 1900, p. 766.

Chauffard and Castaigne* believe that the intermittent secretion results from the inhibitory action on the kidney of certain toxic bodies set free by the liver. Nervous excitement in young subjects is also said to give rise to polycyclic elimination.†

In 46 cases of different affections, Asfalg ‡ found that intermittent excretion occurred in 60 per cent., and that in half of these the excretion was intermittent during the day only.

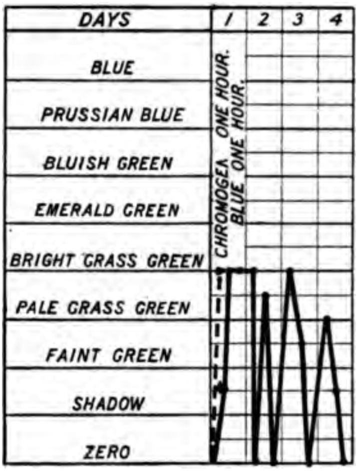

Chart 15.—Intermittent elimination of methylene blue in a case of syphilis. No signs of renal disease. Blue shewn by continuous line, chromogen by dotted line.

In 61 cases under my observation, intermittent elimination was present in 14 (23.3 per cent.). In 6 healthy individuals the elimination was intermittent in all (Chart 16).

The state of the blood and urine during the elimination of methylene blue.—Beyond the fact that methylene blue is transformed into a colourless body, which passes into the blood and is excreted by the kidneys, nothing is known concerning the nature of the body into which the blue is changed. If it were possible to demonstrate the presence of this body in the blood, the measure of the accumulation in the blood would form a valuable means of estimating the functional power of the kidney.

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* *Jour. de physiol. et de pathol. gén.*, 1899, p. 476.

† Pugnat et Revilliod, *Arch. gén. de méd.*, 1902.

‡ *Zeitschr. f. innere Med.*, 1902, 226.

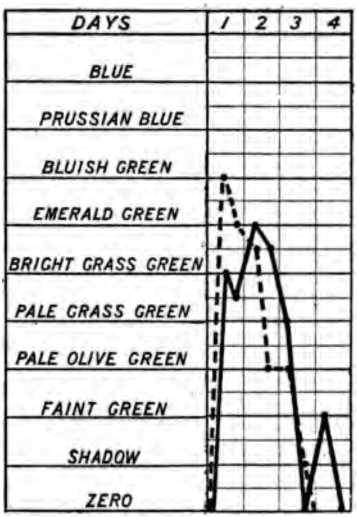

Chart 16.—Intermittent elimination of methylene blue in healthy individual. Single intermission on third day. Blue shewn by continuous line, chromogen by dotted line.

But the blood plasma is not stained, nor can any change in colour of the white corpuscles be detected. The spectroscope shews no change, and the tests which reveal the presence of chromogen in the urine do not demonstrate any such body in the blood.

Albarran has carried out a series of experiments with the object of investigating the nature of the body circulating in the blood. By various means, this observer endeavoured to remove the albuminoid substances which might interfere with the demonstration of the methylene blue, but he failed to demonstrate the presence of blue. He believes that the difficulty rests in the extreme dilution of the blue or chromogen.

That the circulating blood contains this body in quantity is proved by an experiment carried out by this observer. A dog was injected with 1 cubic centimetre of 5 per cent. methylene blue, which appeared in the urine. Four hours later the animal was bled, and 40 cubic centimetres of the serum were injected into another dog, with the result that blue appeared in the urine of the second dog.

Whatever form this circulating dye may take, it is produced at the point of injection. Achard and Castaigne * injected into the peritoneal cavity of a living animal a weak saline solution of methylene blue. After a time they removed the solution and found that it contained chromogen but no blue.

A point of some importance is the seat of the transformation of the circulating chromogen into blue and the nature of the process. In the living body the process of transformation is carried out by two organs only—the liver and the kidney. Neither blue or chromogen appear in any of the other secretions. If an animal in which methylene blue has been injected be killed—the tissues and organs are at first unstained, but after a few minutes they change colour and assume a blue tint. I endeavoured to turn the oxidation of chromogen to use in the living body in order to stain the kidney, with a view to demonstrating to the naked eye on the operating table the amount of epithelial tissue remaining in a diseased kidney. For this purpose I used peroxide of hydrogen as an antiseptic during an exploration of the kidney in a patient in whom I had previously injected 15 minims of methylene blue for the purposes of diagnosis. There was, however, no trace of blue colouring on the cut surface of the kidney or of the muscles at the end of the operation, which lasted

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* *Comptes rendus de la Soc. de biol.*, Dec. 18, 1897, p. 1901.

40 minutes. Yet the urine at the time was deeply stained with blue.

It is uncertain which part of the kidney transforms the chromogen into blue and excretes the blue. Garnier, of Nancy, experimenting on frogs, fixed the blue by molybdate of ammonia, and found that granules of the colouring material could be seen in the protoplasm of the epithelium lining the channels which correspond to the convoluted tubules and the last part of the loop of Henle.

The excretion of a part of the methylene blue as a colourless derivative was first noted by Voisin and Hauser.*

In my cases, the chromogen, almost without exception, commenced to pass in the urine before the methylene blue appeared. In normal subjects the chromogen was usually detected in 15 or 20 minutes from the time of the injection, while the blue began about 15 minutes later. The amount of chromogen rapidly increased and attained a very deep blue colour before the methylene blue had more than tinted the urine with green. The chromogen remained in excess of the blue during the first two hours or so, and then the blue assumed a greater proportion and maintained this throughout the remainder of the test.

When kidney disease was present, both the chromogen and the blue might be delayed, but it might happen that the chromogen delay was slight, while the methylene blue delay was prolonged. The chromogen excretion would then continue for some time before the blue was superadded.

According to Achard and Castaigne,† the diseased kidney eliminates chromogen more easily than blue. They sometimes found in chronic lesions of the kidney at the commencement and at the finish of the elimination a period of varying duration in which only chromogen passed.

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* *Gaz. hebdom.*, May 27, 1897.

† " L'examen clinique des fonctions rénales," 1900.

This corresponds with what I found at the commencement of elimination, but I failed to observe in my cases, with one exception, that the chromogen excretion remained after the blue had disappeared.

It may happen in a case of renal disease that no methylene blue appears in the urine, but after a delay chromogen appears for a short time. Again, both methylene blue and chromogen may be absent from the urine in renal disease.

In three cases Albarran has observed an alternate excretion of methylene blue and chromogen at short intervals.

It appears to me to be doubtful whether the chromogen of the blood is identical with the chromogen which can be demonstrated in the urine. If these were identical one might look upon the proportion of methylene blue to chromogen in the urine as an index of the activity of the kidney in restoring the blue to its original form. The chromogen would thus represent that part which had merely filtered through the kidney unchanged, and the blue that part which had been transformed to its original complete form. The evidence which would support this is not, however, very strong. It may happen that a diseased kidney may be unable to excrete blue, yet it passes chromogen ; but this is not the general rule. Usually, if no blue is passed, no chromogen can be detected in the urine either, and further, the proportion of chromogen does not increase as the methylene blue diminishes in diseased kidneys.

It appears more likely, from the impossibility of obtaining blue from the chromogen of the blood, that it circulates in a different form, and that the chromogen of the urine is produced by the kidney, and is an intermediate form in the process of regeneration of blue from the chromogen of the blood.

A urine stained with methylene blue may sometimes clear on standing, so that no trace of the blue colour remains. If such a urine be shaken it will quickly regain the blue colour.

The change is brought about by the fermentation of the urine, which changes the blue into a leuco-derivative. This is an unstable body, readily transformed into methylene blue by the action of oxygen. It is to be distinguished from the chromogen which is present when the urine is eliminated.

CHAPTER V

ELIMINATION OF CERTAIN SUBSTANCES BY THE KIDNEYS (*concluded*)

The Author's Experience of the Methylene Blue Test—An Estimation of its Value—Indigo-carmine Test—Rosaniline Test—Iodide of Potassium Test—Salicylate of Soda Test—The Toxicity of the Urine

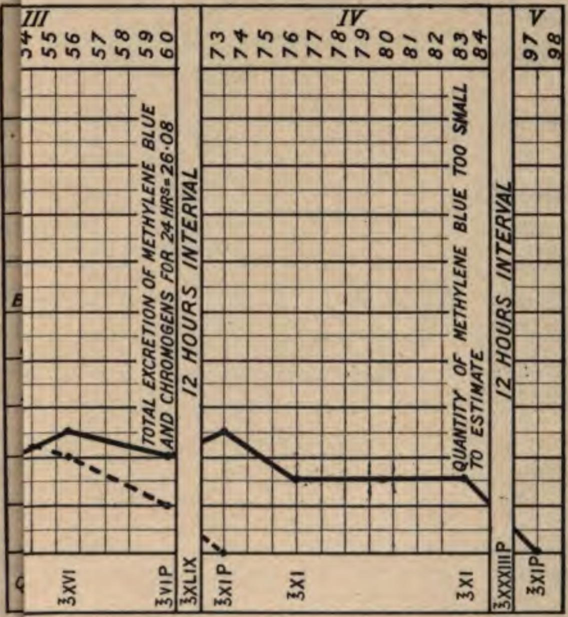
THE AUTHOR'S EXPERIENCE OF THE METHYLENE BLUE TEST

THE 61 cases in which this test was used for the estimation of the renal function form only a portion of the total number of patients upon whom I made observations. In 40 others I administered the blue in the form of a pill. This method of administration shewed some fallacies which were connected with absorption from the intestine, and the time of appearance and the duration of elimination shewed differences from the time and duration with the injection method. I therefore decided not to include these cases, since they could only have led to confusion by necessitating a double normal standard.

In order that I might have a standard for comparison, the test was used on 6 healthy adult men who volunteered themselves for this service. The remaining 55 cases were injected for the purposes of diagnosis, or the blue was administered for its therapeutic effect. The dose in all cases was the same; 15 minims of a 5 per cent. aqueous solution of methylene blue injected into the muscles of the buttock.

Injection of methylene blue in healthy subjects.—The dye in these healthy subjects appeared at the end of 30 minutes as a faint greenish tinge in the urine (Chart 17), with one exception. In this case the visible excretion began at the end of fifteen minutes.

The colour of the urine rapidly deepened to a well-marked green and passing through bright grass green



Cl individual. The total quantity of methylene blue and antity of urine in ounces.

bladder.

The duration of excretion of the blue in these cases was prolonged beyond the 30 to 60 hours given by most

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* *Gaz. méd. des hôp.*, March, 1903.

th one exception. In this case the visible excretion
gan at the end of fifteen minutes.

The colour of the urine rapidly deepened to a well-
rked green, and passing through bright grass green
ched an emerald green colour in from 1 to 4 hours. It
ched its maximum point in 3 or 4 hours (3), or in 15
to 24 (2) hours. During the diuresis following a meal,
blue colour faded for about an hour and then rose
its previous intensity (Chart 17). The blue coloration
not, however, vary so greatly with the changing quan-
of fluid as might have been expected.

Each morning, while the elimination lasted, there was
ise in the quantity of blue in the first urine. In 3 of
healthy individuals the highest point of blue excre-
was reached in the morning urine of the second
In 2 others the quantity of blue equalled that
sed during the height of elimination on the first day.
s may be compared with an observation of Linossier
Lemoine,* who noted that in the recumbent posi-
the elimination of methylene blue might be increased
four or five times.

Muscular exertion in itself does not, however, appear
lead to diminished excretion of blue. One of my
lthy subjects was at the time undergoing a course of
re muscular exercise (wrestling, ju-jitsu), yet the color-
n of the urine was not less intense, nor was the quantity
rapidly excreted, than in the others.

The increase of blue in the morning is not coincident
a corresponding fall in the quantity of chromogen,
hat there was no suspicion that an increased activity
he conversion of chromogen to blue was going on in
lengthened period during which the urine lay in the
der.

The duration of excretion of the blue in these cases
s prolonged beyond the 30 to 60 hours given by most

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* *Gaz. méd. des hôp.*, March, 1903.

observers. The blue was present in the urine during 48, 72, 84, 98, 99 hours and 6 days. The charts shew, however, that the deep blue staining of the urine had passed off in 48, 48, 72, 77, 77, and 72 hours respectively, and that after that time only small quantities, sometimes mere traces, were found. One might therefore use these last figures for comparison with the excretion of patients suffering from renal disease.

In each of the 6 cases the excretion was intermittent in its course. Intermittent elimination of blue has hitherto been looked upon as the result of variation in the hepatic function, and has been said to be characteristic of hepatic inefficiency.* Nervous excitement and hypertrophic changes in the kidney have also been said to cause this disturbed rhythm of elimination. These subjects who submitted themselves to my observation were not suffering from any of these conditions, but were perfectly healthy and in active work. The intermissions occurred after the greater wave of elimination had passed. They might have been overlooked had not careful and frequent records been made. It may therefore be inferred that slight intermissions occurring late in the elimination of blue are compatible with complete renal and hepatic health.

The elimination of chromogen was carefully studied in these cases. In 5 of the cases chromogen could be detected in the urine 15 minutes after the injection; in one 30 minutes elapsed. The chromogen increased rapidly, and reached its point of maximum intensity from ½ to 3 hours after the injection. This was greater than the elimination of blue at any time in 3 cases, and equal to it in the remaining 3. From this point the elimination of chromogen fell rapidly. In 4 cases the chromogen had fallen below the blue by the end of the first 24 hours; in another by 36 hours; and in the last it remained in excess for about 53 hours. An alternate swing of chromogen and blue excretion occurred during the first 12 hours in one case.

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* Chauffard, Cavasse, and Castaigne, *loc. cit.*

The chromogen disappeared from the urine in all these cases while the blue was still present in fair quantity. The interval of time between the disappearance of the chromogen from the urine and the last trace of the blue ranged from 12 to 48 hours.

Injection of blue in disease.—In the 55 cases injected for the purposes of diagnosis, there was evidence in several which suggested that shock and general anæsthesia tend to prolong the interval between injection and elimination, and that conditions, such as age and alcoholism, which are likely to induce or be accompanied by sclerotic changes in the kidneys, may be coincident with prolonged excretion.

In *inflammatory diseases of the bladder*, where there was no reason to suspect renal changes, there was some delay in the appearance of the blue. Of 4 cases of tuberculous cystitis, 3 showed delayed elimination (70 minutes, 1 hour and 50 minutes, 3 hours and 20 minutes). The blue was present in the urine for extended periods (93 hours and 7 days) in 2, in a third elimination was completed in 60 hours, and the urine of the fourth was clear in 41 hours. This last patient had some signs of renal disease.

Cases of *obstruction in the lower urinary tract* invariably shewed a delayed elimination. In 7 cases of stricture the narrowing of the urethra was sufficient to interfere seriously with the outflow of urine (8 F. and under); there was delay in the commencement of elimination in all, the blue appearing in from 1 to 4½ hours. The blue was eliminated well, however, for the urine was deeply stained. Prolonged excretion occurred in two cases (5 days 15 hours, and 6 days 12 hours). In one of these there were symptoms of renal disease, in the other they were wanting. Urea was excreted in normal amount in these cases, but there can be little doubt that some degree of interference with the renal function was present, and that this was correctly indicated by the methylene blue elimination.

In similar manner, enlargement of the prostate, whether simple or malignant, interfered with the excretion of methylene blue. Of 6 cases of simple enlargement of the prostate, 3 shewed signs of renal infection or of back pressure, and 3 shewed no signs of renal disease. Of the 3 cases which shewed signs of kidney disease the elimination of methylene blue was delayed 3 hours in one, and 3 hours and 20 minutes in another, but was normal in its time of onset in the third. The urine of the last case contained blue for 5 days, and in one of the other cases the elimination was prolonged for 8 days and 7 hours, while the third completed the elimination in 40 hours. The quantity eliminated by these patients was satisfactory. Of the 3 cases in which signs of renal implication were absent one commenced to excrete blue in 30 minutes, and continued for 116 hours. A second case is noted as having an unusually pallid complexion and diminution in the total elimination of the urea. There was a delay of 4½ hours in the commencement of secretion, and the urine was stained for 78 hours. The third case, in which no renal symptoms were present, eliminated neither methylene blue nor chromogen after two separate injections. I shall refer to this case again.

In 4 cases of malignant disease of the prostate there were no symptoms of renal inefficiency in 3, and in the fourth the symptoms were insignificant (loss of appetite and weight). The residual urine in these cases varied from 2 to 10 ounces.

In all these cases there was delay in the commencement of elimination (3 hours, 4½ hours, 8 hours, and 8 hours). The urine was stained a deep blue in each case. The duration of elimination was prolonged, and the prolongation was correspondingly great where the delay was marked.

Thus the case with 3 hours' delay excreted blue for 88 hours, that with 4½ hours' delay continued for 96 hours, and in the two cases with 8 hours the elimination was prolonged for 6 days each.

The delay in commencement and the prolonged excretion in these cases of prostatic disease was in some measure related to the quantity of residual urine, as the cases in the accompanying table shew:—

	Commencement of blue elimination.	*Duration.*	*Ounces of residual urine.*	*Symptoms of kidney disease.*
a.	8 hours	6 days	10	None
b.	2½ ,,	5 ,,	11	Slight
c.	3 ,,	3½ ,,	2	None
d.	8 ,,	4½ ,,	16	Signs
e.	No elimination of blue	—	Complete retention	Slight
f.	8 hours	6 days	10	None
g.	4½ ,,	84 hours	0	None
h.	40 minutes	5 days	0	Slight

The average time of appearance of blue in these 17 cases of obstruction in the lower urinary tract was 3 hours and 27 minutes, while the average duration of the elimination was 100½ hours, without taking into consideration one case in which no blue was passed. The delay was more marked, and the period of elimination more prolonged, where the obstruction was due to enlarged prostate than when it was due to stricture. Thus, in the 8 cases of stricture the average time of commencement was 2 hours and 16 minutes, and the average duration 8½ hours; whereas in the cases of prostatic obstruction the average delay was 4 hours and 25 minutes (excluding the case where no blue appeared), and the average elimination continued for 118½ hours.

In one of the cases of enlarged prostate there was a delay in commencement of elimination of 8 hours, and the urine was tinged for 4½ hours. The colour did not exceed a dirty green. Nine weeks after suprapubic cystotomy a second injection was made and the blue commenced in 3 hours and continued for 40 hours.

This case is worthy of more extended notice.

G. B., a worn-looking man of 52 years, attended St. Peter's Hospital complaining of suprapubic pain and frequent and difficult micturition, of 12 months' duration.

He passed water 5 times daily in a small, feeble, intermittent stream, and he rose twice at night. There was no renal pain or tenderness. His complexion was pallid, with a malar flush. He had lost 2 stones weight in the past 12 months, and was very feeble. There was no disease of the heart or lungs. He did not complain of headache or thirst, and his tongue was moist.

The prostate was enlarged, elastic, and freely movable. There were 36 ounces of residual urine in the bladder. The urine was pale, with a specific gravity of 1010 and a faint cloud of albumin. The quantity passed in 24 hours was 82 ounces, with 1.3 per cent. of urea.

Methylene blue shewed a delay in commencement of elimination of 8 hours, and the blue continued to stain the urine for 4½ hours. The colour did not exceed a dirty green. The patient was considered to be too ill for prostatectomy, and the bladder was drained suprapubically. For 4 days after the cystotomy he was very drowsy, with a dry tongue and a dry, harsh skin. The quantity of urine that drained away was excessive. The temperature was 101.6 on the day following the operation, and fell to 99 on the fifth day. From this time a gradual improvement took place. Nine weeks after the cystotomy the patient's condition had much improved. His tongue was moist, and he was increasing in weight. The urine was amber coloured, specific gravity 1016, faintly alkaline, and contained a trace of albumin.

An injection of methylene blue stained the dressing of the cystotomy wound in 3 hours, and the elimination continued for 40 hours. I decided to remove the prostate, and enucleated with some difficulty a small bilobed prostate with an intravesical projection. The patient was drowsy for the first 24 hours after the operation, but after that his convalescence was uninterrupted.

This case forms an excellent illustration of the improvement that takes place in the renal function after the drainage of an obstructed bladder.

Primary disease of the kidney.—The permeability of the kidneys to methylene blue was studied in a series of cases where renal disease of varying severity was unconnected with disease of the lower urinary tract.

In two of three cases where nephrotomy had been performed at a previous time without any gross lesion being discovered, the commencement of elimination was delayed (3¾ hours), but the quantity passed was satisfactory. In the third case the excretion commenced promptly, but the urine only contained sufficient dye to stain it a pale green. The duration was within the normal limit in all these cases, and the chromogen shewed no abnormality.

In 3 cases calculi had been passed from the kidney. In each of these cases there was a delay in the commencement of elimination (43 minutes, 1 hour, 1¾ hours). All of them passed urine of a deep emerald green colour, and in two the excretion was slightly prolonged.

In 3 cases there was pyelitis of unexplained origin. In each the commencement of elimination was delayed (1 hour, 58 minutes, 1 hour), the quantity of blue eliminated was satisfactory, and the course was intermittent in two cases and constant in one. In one of the intermittent cases the blue remained in the urine for 96 hours.

In one patient who suffered from partial suppression of urine, with abdominal distension, vomiting, hiccough, dry skin, and dry, glazed, red tongue, after a renal exploration there was a delay of 58 minutes in the onset of elimination, the urine was stained green, but this did not become dark. The duration of the excretion was 48 hours.

In 7 cases there was advanced disease of one or both kidneys. Three were cases of calculous disease, in 2 of which large, irregular calculous masses could be felt through the abdominal wall, while in the third a large firm kidney could be palpated. There was one case of extensive hydronephrosis, one of tuberculosis of the kidney, one of pyonephrosis complicating urethral stricture, and one of bilateral suppurative pyelonephritis.

Of the renal calculus cases methylene blue appeared in the urine in one at the end of 27 minutes, and a dirty green colour was maintained for 72 hours. The time of commencement and the duration were normal, but the quantity was reduced.

In a second stone case three injections at different periods failed to produce any staining of the urine and no chromogen appeared.

In a third case the methylene blue appeared in 1 hour 50 minutes, the urine was green in colour for 18 hours, and the chromogen appeared in 25 minutes, and reached a deep green colour. A successful nephrectomy was performed.

In the fourth case there was urethral stricture and a large pyonephrosis, no blue appeared in the urine, but chromogen was found in 1¼ hours, and rose to a green colour lasting 84 hours. This case will be discussed more fully.

The fifth case was a man aged 42, with a large hydronephrosis occupying one-half of his abdomen. Excretion of blue was delayed for an hour after injection, and the elimination was continuous and lasted 40 hours.

The urine in this case had a specific gravity of 1020, and contained 2 per cent. of urea in 40 ounces of urine *per diem*. The patient had lost weight, and his complexion was sallow. He had suffered habitually from sickness from the pressure of the hydronephrosis. There were no marked signs of renal disease. Nephrectomy was performed. For 4 days the patient was drowsy and very weak, with a running pulse. The quantity of urine was small, but gradually rose from 18 ounces to 34 ounces in 24 hours. The drowsiness passed off, and the patient made a good recovery.

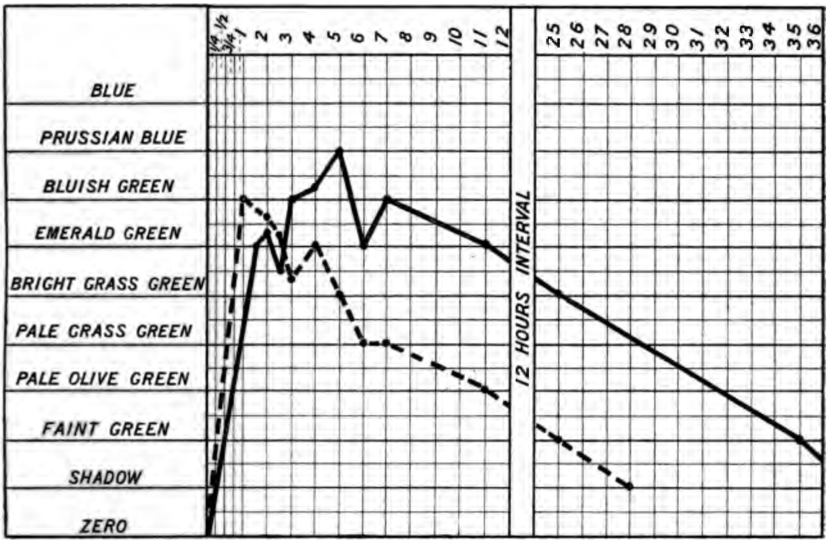

Chart 18.—Elimination of methylene blue in tuberculous kidney. Delayed commencement and rapid short elimination.

The sixth case was a girl of 20, suffering from tuberculous cystitis and a tuberculous kidney on the left side. Methylene blue appeared in the urine in one and a half hours after the injection, pursued a continuous course, and disappeared in 40 hours. The chromogen was present in normal quantity. The urine contained 1.4 per cent. of urea in 45 ounces. After nephrectomy the elimination of the methylene blue remained practically the same as before the operation (Chart 18).

The seventh case was a man with prostatic abscess, cystitis, and advanced suppurative pyelonephritis. No blue and no chromogen appeared in the urine.

There were two cases in which nephrectomy had been performed three years and three and a half years previously.

A pyonephrosis had been removed in one patient, and when he came under my observation a large calculus was discovered in the lower segment of the ureter on the side from which the kidney had been removed. The urine was alkaline, with a specific gravity of 1020 and a heavy stringy deposit. Albumin and some pus were present. The urea amounted to 3 per cent. in the 28 ounces secreted in 24 hours. He shewed no signs of renal insufficiency. Blue appeared in the urine in 35 minutes, was present continuously for 50 hours, and then it disappeared. The chromogen did not persist after the urine had cleared. The calculus was removed extraperitoneally through an incision above and parallel to Poupart's ligament. The operation lasted 75 minutes, and the patient made an uninterrupted recovery.

In the second case I had removed a large hydronephrosis of the left kidney, together with the ureter containing a calculus, in 1903. The patient was in good health, and beyond an occasional slight pain in the remaining kidney, there was no sign of deficient renal function. Methylene blue appeared in 45 minutes in the urine, and chromogen was excreted in good quantity. The elimination was continuous, and lasted 4 days.

Cases in which no blue was eliminated.—There were 4 cases in 61 where blue did not appear in the urine, and these will be more fully considered. They were cases of bilateral renal calculus, of pyonephrosis complicating stricture of the urethra, of urinary obstruction from enlarged prostate and of pyelonephritis with abscess of the prostate and cystitis. I operated on three of these cases and refused operation in one.

The patient who was refused operation suffered from advanced bilateral calculous disease, and died of suppression of urine 18 months later. The case was briefly as follows:—

R. S., aged 46, had suffered from symptoms of stricture six years before I saw him, and had undergone internal urethrotomy. Previously to this he had passed several stones. After the operation he suffered from pain in both kidneys, more especially on the left side. He had several attacks of renal colic on the left side, and after one of these passed blood. Two years ago he had passed a calculus the size of a plum-stone. Since that time he had had an attack of renal colic on the left side about once a month. There was a severe pain in the hollow of the right foot during one of these attacks of colic. He had not lost flesh, nor had he suffered from headaches. He complained of constant thirst. The patient was a spare, sallow man, able to attend to his business as publican, but had not been strong or inclined for active exercise for some years. His skin was dry and harsh, and he seldom perspired. His tongue was moist and clean, and his appetite fair. There was no œdema.

The urine was alkaline and stinking, with a specific gravity of 1014, and showed a heavy deposit of pus with numerous shreds. The right kidney was readily felt as a hard, irregular, stone-like mass, having a prominent nodule on its anterior surface. It moved with respiration, and was somewhat tender to touch. The left kidney was not palpable, but was occasionally tender.

Cystoscopic examination showed cystitis. The ureters were slit-like when closed, and gaped widely to emit a sluggish stream of murky urine. A radiograph shewed a large calculous mass in the right kidney, and several calculi in the left kidney. Three injections of methylene blue at different periods failed to produce any staining of the urine, and no chromogen was found. On this evidence I refused to operate.

Eighteen months later the patient became sick and constipated. He became increasingly drowsy, and the quantity of urine secreted fell gradually during fourteen days, when he died.

Of the 3 cases that were submitted to operation, 2 died.

In one of these the operation was done to relieve a large collection of pus in the prostate when the patient was beyond the hope of recovery. The other 2 cases were operated on in the hope of cure.

The patient with enlarged prostate (for details of this case, C. S., *see* page 5) shewed no symptoms of renal inefficiency before operation. He was a spare, muddy-complexioned man, who had suffered from complete retention for some months. The urine had a specific gravity of 1010. There was an increased quantity of urine, and the urea varied from 0.6 to 1.1 per cent. The temperature occasionally rose to 100° F. Injection of methylene blue produced no change in the urine, and no chromogen was passed. The operation presented no difficulty, and the enucleation lasted three and a half minutes. After operation the urine gradually failed, and the patient died on the fifth day.

The third case that was submitted to operation recovered. This was a case of stricture and pyonephrosis, where methylene blue failed to appear in the urine after nephrotomy, and after nephrectomy the injection of blue was followed by the appearance of chromogen and later of blue in the urine. This affords striking illustration of the abolition of a depressant reno-renal reflex by nephrectomy.

The notes of the case are as follows :—

J. R. had experienced two attacks of cystitis, 10 years and 5 years ago. In the second attack he had passed some small calculi. Two years ago his urine again became foul, and he had frequent and painful micturition. On admission to St. Peter's there was a stricture of the urethra. Urine was passed with difficulty every two hours during the day and hourly at night, in a thin twisted stream. It was alkaline, and contained much pus.

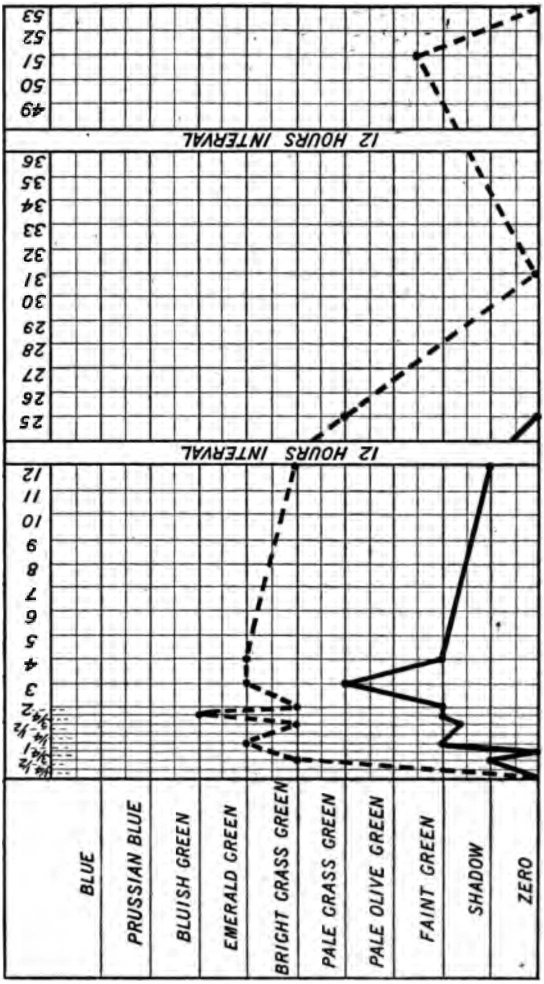

Chart 19.—Pyonephrosis. Elimination of blue (continuous line) and chromogen (dotted line) after nephrectomy. Neither blue nor chromogen appeared in the urine in a previous test before nephrectomy.

The patient was a stout, flabby man. He had lost 2 stones weight, but shewed no symptoms of renal disorder. The left kidney was much enlarged and readily felt through a thick abdominal wall. It was tender to the touch. Internal urethrotomy was performed, and the bladder drained by catheter. The cystitis, however, continued. An injection of methylene blue stained the urine in 3 hours, and elimination was over in 23 hours, a marked delay and short duration. His urine continued alkaline and purulent, the specific gravity was 1020, and the urea 2 per cent. in 56 ounces.

The patient was in too unsatisfactory a condition for any severe operation. Nephrotomy was therefore performed on the left kidney and a large quantity of pus and some small calculi were removed. Twelve days later a second trial of methylene blue was made. No blue was passed in the urine, nor did any appear in the urine which leaked from the wound. Chromogen was found in the urine 1¼ hours after the injection, and rose to a green colour, lasting 84 hours altogether.

After the nephrotomy the patient's condition improved, so that 14 days later I felt justified in performing nephrectomy. After the operation there was a good deal of abdominal distension, and the patient was restless and vomited, but these symptoms passed off.

A third injection of methylene blue shewed a further improvement in the renal permeability. Chromogen appeared one hour after the injection and blue 1½ hours. The urine became a well-marked green for 28 hours. The excretion of chromogen was intermittent. It was present in greater quantity than the blue, and disappeared with it in 28 hours, reappearing in 40 hours for a few hours (Chart 19).

Value of methylene blue tests.—The value of methylene blue as an indication of the state of the renal function must be judged by a comparison with the information obtained from the symptoms and the examination of the urine.

Three out of 8 cases of stricture shewed insignificant symptoms of renal inadequacy; in all, the excretion of urea was large. In all of the cases there was delay, and in several prolongation of blue elimination. The cases were selected as having suffered from intractable stricture for long periods, and belonged to the class of case in which renal changes are common. In these cases the methylene blue appeared to be a more accurate test than the symptoms or the quantitative estimation of the urea. In 11 cases of prostatic obstruction there were insignificant symptoms of renal inadequacy in three and fairly marked symptoms in one case. Delay and prolonged elimination of blue were invariable.

The cases, already quoted, of complete suppression of blue when no symptoms of renal inadequacy were present, may be taken as an illustration of the more accurate indication of the renal function by methylene blue. In 2 of the cases of kidney disease there were general symptoms of renal inadequacy; in one this was only continuous thirst, in the other the symptoms were well marked. In these cases no blue was passed. In the other 2 cases, where no symptoms of renal failure were present and no blue was passed, one died after the operation and had advanced interstitial changes in the kidneys, and the other developed grave symptoms of renal failure after the operation, but these passed off. In one case there was a very marked improvement in the elimination of blue after the removal of a large pyonephrosis, and this was attributed to the removal of a reno-renal reflex inhibition.

The test is, I believe, one which is more trustworthy than the quantitative examination of the urea, or the appearance of general symptoms of renal inadequacy. And this is specially the case in the more severe grades of kidney disease.

It has been urged in criticism of this method that the formation of chromogen introduces an element of uncertainty into the test. The chromogen should be converted into blue when the quantity of the dye is estimated. The elimination of the blue by the liver appears to me to be a more serious disadvantage, and one which cannot be overcome.

Lépine* has drawn attention to a fallacy which underlies observations on this and similar methods. The kidney does not eliminate all bodies without distinction in the same manner, and data obtained from the elimination of one body may not be reliable when applied to another. It is undoubted, however, that there is a certain parallelism in the elimination of different bodies, and that the general permeability of the kidney for most bodies which it excretes is approximately similar to that for methylene blue.

INDIGO-CARMINE TEST

Indigo carmine was used by Heidenhain† in his well-known investigations into the function of the kidneys in 1874, but it was introduced into clinical medicine as a test of the renal function by Voelcker and Joseph‡ in 1903. These authors claimed that the injection of indigo carmine was innocuous, and that it was rapidly excreted by the kidneys without the formation of a colourless derivative or chromogen. In their earlier work they injected 4 c.c. of a 4 per cent. solution of indigo carmine into the muscles of the buttock. They found, however, that a solution of this strength was not a true solution, but a suspension of particles of indigo carmine. They therefore used a solution of 0.4 per cent. strength and injected 20 c.c. of this.

Indigo carmine, if injected in large quantities, is excreted also by the liver, and is found in the fæces as a leuco-derivative which becomes transformed into blue on exposure to air. About a quarter of the total amount of indigo carmine is passed in the urine, while the greater part cannot be traced.

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* *Lyon méd.*, Feb. 20, 1898.

† *Arch. f. Physiologie*, B. ix., 1874.

‡ *Münch. med. Woch.*, 1903.

The quantitative estimation of indigo carmine in the urine is carried out in the same way as that described for methylene blue.

In healthy kidneys, after injection of 20 c.c. of 0.4 per cent. solution of indigo carmine the urine becomes tinged with blue in about 5 minutes, and the excretion reaches its highest point half an hour to three-quarters of an hour after the injection. It then falls gradually and disappears in about 12 hours.

A delay in the commencement of the elimination and a diminution in the quantity of dye eliminated are indications of a reduced renal function.

The dye is decolourised by purulent alkaline urine. Kapsammer,* using 4 c.c. of a 4 per cent. solution, found that the urine became green in from ten to twelve minutes, and that delay occurred when renal disease was present. The delay was proportional to the extent of the disease.

The intensity of the colouration was also important. The duration of the elimination was, on an average, 24 hours, but variations occurred in healthy individuals.

ROSANILINE TEST

Lépine† proposed the use of rosaniline as a substitute for methylene blue. Fifteen minims of a 1 per cent. solution of rosaniline trisulphate of soda are injected. Pugnat and Revilliod‡ have used the same quantity of a 5 per cent. solution. The red colour appears in half an hour, and reaches its maximum about the third hour. The whole elimination is finished in 24 hours. The colour of the urine may be intensified by the addition of a few drops of hydrochloric or acetic acid.

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* "Nierendiagnostik und Nierenchirurgie," 1907.

† *Lyon méd.*, 1898, 251–573.

‡ *Arch. gén. de méd.*, 1902, 19.

According to Dreyfus,* from 80 to 97 per cent. of the dye is eliminated, and anything below 75 per cent. shews a diminished permeability of the kidney. The quantitative estimation is carried out in a manner similar to that of methylene blue.

Certain differences from methylene blue are observed. No chromogen is found, no oscillations are observed in the course of the excretion, and the elimination is over in 48 hours. The variations of elimination brought about by diseases of the kidneys correspond very closely to those observed in methylene blue.

IODIDE OF POTASSIUM

Variations in the elimination of iodides during the ingestion of iodide of potassium in diseases of the kidneys have been observed, and much has been written upon the subject. The earlier work was carried out rather with reference to the accumulation of the drug in the body and the production of iodism than with the idea of measuring the function of the kidney. Duckworth† was early in the field, and contributed an important paper in 1867 on the elimination of this and other substances by the kidneys. In a monograph published in 1893, Lafay‡ gives over 350 references upon the subject. This author made a systematic investigation of the elimination of the drug in the urine. Bard and Bonnet§ contributed further observations. Desprez‖ introduced the method of hypodermic administration of the drug.

Iodide of potassium is very diffusible and passes rapidly into the urine, so that no observations of value can be made in regard to the time and commencement of the elimination. The duration of the elimination varies with the dose. A subcutaneous injection of 4 centigrammes should be eliminated in 24 hours. During this time a healthy individual will eliminate from 18 to 29 milligrammes of iodide. When the iodide is administered by mouth the variation in the quantity eliminated by the kidneys may be considerable. About 60 to 70 per cent. of the quantity ingested is passed in the urine, but it may vary from 35 to 99 per cent.*

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* Thèse de Lyon, 1898.

† *St. Bartholomew's Hosp. Rep.*, vol. ii., p. 216.

‡ "L'élimination urinaire de l'iode," Paris, 1893.

§ *Arch. gén. de méd.*, Feb., March, April, 1898, vol. i., p. 129, 282, 464.

‖ Thèse de Lyon, March, 1884.

According to Desprez, the quantity of iodides eliminated in pathological conditions of the kidneys is reduced to one-fifth or one-eighth of the quantity of salt injected. Lafay states that a small dose of potassium iodide will be eliminated in the urine as iodide of sodium, a larger dose partly as iodide of sodium and partly as iodide of potassium, and a large dose (15 to 50 grammes daily) will be eliminated almost unchanged.

Several methods have been used to estimate the quantity of iodide eliminated in the urine.

Struve's method is recommended by Bard and Bonnet. It is carried out as follows. From the specimen to be examined, 50 cubic centimetres are measured and evaporated in a sand bath, after the addition of 5 cubic centimetres of normal saline solution. The residue is charred and then dissolved in water and brought to the boil, adding chlorhydrate of ammonia until the fluid is no longer ammoniacal and the reaction is neutral. The fluid is filtered, the filtrate washed in water, the fluid thus obtained placed in a vessel and 5 cubic centimetres of sulphide of carbon added, and then nitric acid drop by drop. When the addition of a fresh drop of acid does not deepen the colour of the sulphide of carbon the fluid is put into a test tube. It only remains to compare it with different standards of graduated colours previously prepared with a known quantity of iodide of potassium. Tubes may be obtained corresponding to 0.1 milligrammes, 0.2 milligrammes, 0.3 milligrammes, etc.

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* Duchesne, Thèse de Paris, 1884–5.

The important point is to ascertain if the elimination is rapid and in quantity, or if it is slow and prolonged, and a fairly exact idea may be obtained by noting the quantity eliminated in the first 24 hours.

SALICYLATE OF SODA

Pugnat and Revilliod* have studied the elimination of salicylate of soda after hypodermic injection.

One cubic centimetre of a solution of 30 per cent. of salicylate of soda is injected hypodermically. Cocaine is added to the solution, the pain caused by the injection being considerable.

The salicylate of soda can be detected in the urine a quarter of an hour after injection, reaches its maximum in the third hour, and continues for 8 to 10 hours. The quantity eliminated varies from 3 to 15 centigrammes, and the greater part of this is passed in the first 5 hours.

The quantity passed during this time is less in interstitial nephritis, but there is little change in parenchymatous nephritis.

THE TOXICITY OF THE URINE

Professor Bouchard† introduced the method of estimation of the toxicity of the urine as a means of determining the power of the kidney to eliminate the poisons produced by metabolism.

This method attributes to the kidney as its most important function the removal of certain substances from the blood which, if retained, would cause auto-intoxication. The normal urine is highly poisonous, but the exact nature of the poison is unknown. The injection of a certain quantity of urine into a rabbit causes symptoms of poisoning, and after a varying interval the animal dies.

For rabbits the lethal dose of normal urine is stated at about 40 to 50 grammes per kilo of body weight. Variation in this dose is stated by Bouchard to be due to retention of poisons in the body from which the urine is derived, and diminished or, on the other hand, increased excretion of poisons in the urine.

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* *Arch. gén. de méd.*, 1902, p. 19.

† "Léçons sur les autointoxications," Paris, 1887; and *Gaz. hébdom. de méd. et chir.*, 1886.

Bouchard injected the fluid into the veins of the ear in rabbits. Modifications of this method have also been suggested. Thus the urine has been injected into the cellular tissues and the serous cavities; it has also been administered by the mouth. Intracerebral injection has been used by Widal, Sicard, and Lesné.*

Two methods of procedure have been adopted. A given quantity of urine has been injected into a rabbit, and the resulting toxic symptoms observed (Jaffroy and Servaux), or a quantity of urine necessary to kill the animal during the course of the experiment is injected intravenously (Bouchard).

The method of Bouchard is that which is most readily applicable, and has been used by most observers.

The quantity of urine which must be injected per kilogramme of body weight to bring about a fatal result is named a "urotoxie." The urotoxic coefficient is the quantity of "urotoxies" that an individual produces per kilogramme of body weight in 24 hours.

The urine should be injected soon after it is passed, for Bouchard points out that urine becomes more toxic when it has been passed some time.

The method is open to many objections. Different urotoxic coefficients have been found for normal urine by many different observers. Thus Bouchard states that the "urotoxie" of a normal individual corresponds to 45 cubic centimetres, Bernard places it between 20 and 35 cubic centimetres, Mairel and Bosc indicate 67 cubic centimetres, and Guinard has found the "urotoxie" to be 130 cubic centimetres.

C. Bruin,† of Naples, states the lethal dose for intravenous injection as 16 to 24 c.c. per kilogramme of body weight of a rabbit, and for intraperitoneal injection as 60 to 90 c.c. per kilogramme. He has been able to immunise rabbits by intraperitoneal injections of urine so that they could withstand 1 or even 2 doses which would be lethal to other rabbits. He states that the serum of these animals will confer a certain degree of immunity if injected into other rabbits.

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* Thèse de Paris, 1899.

† *Comptes rendus XIII. Congrès Internat. de méd.*, 1900.

So great a variation in the figures given for the normal urine must, in itself, destroy any hope of obtaining consistent results in diseased conditions. But further fallacies have been brought to light. Varying results have been obtained in experimenting with the same urine by varying the rapidity of the injection and the pressure under which it is made. In order to eliminate this fallacy the same conditions must surround each experiment.

Again, some of the animals die, not from the toxic effect of the urine, but from the formation of thrombi, and it is necessary to make a careful *post-mortem* examination in order to ascertain whether intracardiac coagulation has thus been caused. It has been suggested that substances which prevent coagulation should be injected in order to avoid this possibility.

It is said that the urine having a different isotonic value from the serum causes alterations in the red blood corpuscles, and thus brings about the death of the animal by plasmolysis, apart from the actual toxicity of the urine.*

Claude, and Balthazard,† and Lesné ‡ have suggested that the fluid should be corrected to the same point of molecular concentration as the blood. This objection does not, however, appear to be of very grave import, and Bernard considers that it may be neglected.

The following are the calculations necessary to determine the toxicity of a urine :—

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* Vaquez and Bousquet, *Presse méd.*, 1899, April 5.
† *Jour. de phys. et de pathol. gén.*, 1899, May 15.
‡ Thèse de Paris, 1899.

If N is the quantity of urine necessary to cause the death of a rabbit and P the weight of the animal, then

$$\frac{N \times 1000}{P} = T.$$

T is the lethal quantity of urine per kilogramme of the animal. This is the unit of toxicity, the "urotoxie."

The number of "urotoxies" eliminated by the individual in 24 hours will be obtained by the following formula :—

If Q represents the quantity of urine of the 24 hours, $\frac{Q}{T} = U$, the number of "urotoxies" eliminated in 24 hours.

In order to obtain the *urotoxic coefficient* of Bouchard, the quantity of "urotoxies" per kilogramme of body weight of the individual each 24 hours the following formula is used :—

PP is the weight of the individual, and U is the number of urotoxies of the urine of 24 hours.

$\frac{PP}{U}$ = the urotoxic coefficient.

This coefficient is normally about 45, but it varies within wide limits.

Most observers who have used the method are agreed that so long as the figures are not considered to be mathematically exact, the estimation of the toxicity of the urine is likely to afford useful information. If the toxicity of the urine be considered alone, without reference to that of the blood, it does not give any adequate idea of the work of the kidney in eliminating toxic substances.

When a comparison is instituted between the toxic properties of the urine and the blood some more precise data in regard to the work of the kidney might be obtained. Tarnier and Chembrelent have examined the blood in women suffering from puerperal eclampsia,* and found an inverse ratio between the toxicity of the blood and that of the urine, and Bar and Rénon* have obtained similar results. These results have not, however, been corroborated by other observers. Albarran† was unable to prove in several cases of pyelonephritis that the blood was more toxic and the urine less, while Bernard only found an inverse ratio of toxicity of the two fluids in 4 out of 21 cases.

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* *Ann. de gynécol.*, 1892, p. 321.

Roger ‡ refers to "the complexity and instability of the composition of the serum, phenomena which interfere with the estimation of their toxicity."

It has further been shown by Achard, Castaigne, and Loefer§ that the toxicity of the urine is not equivalent to that of the blood, nor the latter to the toxicity of the tissues.

The blood tends to maintain a constant composition, and the accumulation of substances not eliminated by the kidneys takes place not in the blood but in intimate relation with the tissues themselves.

Thus precise conclusions in regard to the permeability of the kidney cannot be drawn from a comparison of the toxicity of the urine and the blood.

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* *Gaz. hèbdom. de méd.*, 1897, p. 494.

† "Exploration des fonctions rénales," 1905.

‡ *Presse méd.*, 1895, p. 109.

§ "Maladies des reins," Debove, Achard et Castaigne, p. 906.

CHAPTER VI

THE GLANDULAR FUNCTION OF THE KIDNEY

The Phloridzin Test—Technique of the Test—The Test in Renal Disease—Value of the Test

THE manufacture of hippuric acid from benzoic acid and glycine is the only synthetic process that is known to take place in the kidney. The main supply of benzene derivatives from which this body is formed is to be found in vegetable and fruit food. Upon a mixed diet the excretion of hippuric acid in human urine amounts to about 0.7 gramme per diem. Upon a diet rich in fruits it may be raised to three or four times this quantity.*

Renal disease does not apparently affect the elimination of hippuric acid.† Achard and Chapelle, however, injected subcutaneously one gramme of benzoate of soda (corresponding to 1.24 grammes of hippuric acid). The quantity of hippuric acid in the urine in 24 hours was increased by 1.12 grammes and 1.16 grammes in two healthy subjects. In two cases of interstitial nephritis it was only raised .699 gramme and .440 gramme; in other cases of renal sclerosis, scarlatinal nephritis, and during uræmic convulsions, it increased only .210 grammes.

No observations of clinical value have been made in regard to the renal function by this means.

It is known that a chemical change takes place in the kidney on the injection of phloridzin, and that its administration is followed by a temporary glycosuria which is influenced by diseases of the kidneys.

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* F. Gowland Hopkins, in Schäfer's "Text-book of Physiology," vol. i., p. 601.

† *Gaz. degli Ospedali et della Clin.*, 1898, No. 145.

J

THE PHLORIDZIN TEST

Phloridzin is a glucoside obtained from the root bark of the pear, the apple, or the cherry tree. It contains 38 per cent. of dextrose, which may be split off by boiling with acids, leaving a substance called phloretin.

Von Mering* discovered that the ingestion of phloridzin caused glycosuria. The glycosuria lasts for a few hours and then passes off, unless the dose is repeated. In well-fed animals the amount of sugar excreted varies considerably, but it is more constant during starvation.

The amount of sugar excreted does not depend upon the dose of phloridzin injected, provided sufficient is given to produce the maximal effect, and the dextrose in the urine cannot therefore be derived from that of the phloridzin. The source of the sugar is apparently the tissue proteid.

Von Mering supposed that the kidney was rendered more permeable to dextrose by the action of the phloridzin, so that the normal sugar of the blood passed into the urine. There was, however, no hyperglycæmia in animals dosed with phloridzin, but rather a diminution in the normal glycæmia, and Minkowski suggested that the diabetes was purely renal in origin.

According to Minkowski,† the phloridzin was split up by the renal cells into dextrose and phloretin, the former being passed into the urine and the latter passed back into the blood, where it combined with the blood sugar to form phloridzin again, and this was again split up by the renal cells. Some part of the phloridzin escaped into the urine, so that the process ceased after a time.

Zuntz‡ has shewn that if phloridzin is injected into the renal artery of one kidney the urine of that kidney contains sugar before the urine of the opposite kidney. The action of phloridzin is therefore located in the kidney.

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* *Centrabl. f. d. med. Wissensch.*, 1885, S. 531; *Verhandl. der Congress f. innere Med.*, 1886, S. 185, 1887, S. 349; *Zeitschr. f. klin. Med. Berlin*, 1888, xiv., S. 405, 1889, xvi., S. 431.

† *Archiv f. experiment. Pathol. u. Pharmak.*, 1893, B. xxxi., 137.

‡ *Dubois Archiv*, 1895, 570; *Verhandl. der physiol. Gesellsch. zu Berlin*, 1894, S. 51.

More direct proof was afforded by the experiments of Biedl and Kolisch,* who found that when kidneys isolated from the body were supplied with defibrinated blood containing phloridzin the urine they produced contained sugar. "In this respect the kidney comes to act like the mammary gland. Its cells form sugar out of the non-saccharine constituents of the blood. Phloridzin would seem to confer secreting powers on the renal cells, in other words, to make the kidney in part glandular in function." (Moore.)†

This is based upon three facts. Diuretics do not increase phloridzin diabetes in the same manner as they increase the glycosuria in those forms of diabetes in which hyperglycæmia exists. Mechanical or irritative injuries to the kidney diminish its power of secreting a saccharine urine with phloridzin.‡ Necrotic changes take place in the cells of the uriniferous tubules after prolonged excessive phloridzin administration.§

Klemperer|| was the first to apply this knowledge to clinical medicine. He shewed that phloridzin diabetes was absent when the drug was administered in cases of chronic nephritis.

Magnus Levy¶ disputed the statements of this observer, and held that if phloridzin were injected subcutaneously, instead of by the mouth as in Klemperer's observations, the glycosuria was produced in cases of nephritis as in healthy individuals.

Achard and Delamere** carried the matter a step further and introduced the drug into the field of practical medi-

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* Quoted by Pavy, Brodie and Siau, *Journ. of Physiol.*, 1903, p. 467.

† "Recent Advances in Physiology and Biochemistry," 1900.

‡ Richter, *Zeitschr. f. klin. Med.*, B. 41, 1900, and Pavy, Brodie and Siau, *loc. cit.*

§ Kossa, *Zeitschr. f. Biol.*, 1900, S. 324; Seelig, *Deut. med. Woch.*, 1900, S. 707.

|| *Verhandl. des Vereins f. innere Med. zu Berlin*, 1896; and *Archiv f. exp. Pathol.*, 1897.

¶ *Verhandl. des Verein f. innere Medicin*, 1896.

** *Bull. et Mém. de la Soc. méd. des hôp.*, April 7, 1899, p. 379.

cine as a test of the renal function. These authors held that the sugar production was dependent upon the functional activity of the kidneys, and that any variation in the glycosuria must mean a departure from the normal function of the kidney. The value of estimating the total excretion of sugar and the necessity for an exact dosage smaller than that previously in use, were the points on which these observers insisted.

Technique of the phloridzin test.—A subcutaneous injection of 15 minims of phloridzin solution (1 – 200) is made. This corresponds to 5 milligrammes of phloridzin.* There is a difficulty in keeping the phloridzin in solution in this degree of concentration, and the addition of carbonate of soda increases the solubility. I found it necessary, however, to use a weaker solution (1 – 400), and to inject a correspondingly greater quantity. The solution must be freshly prepared. It soon becomes discoloured, and the results obtained by old solutions are unreliable.

Sugar can usually be detected in the urine in a healthy individual in 15 minutes, sometimes it does not appear for 30 minutes after the injection. The sugar rapidly increases in amount, and the glycosuria is at its height from ¾ to 1 hour after the injection. It then falls rapidly, and has usually ceased in from 2 to 2½ hours. An injection of 5 milligrammes of phloridzin will normally produce from 1 to 2 grammes of glucose.

I found it convenient to make quantitative observations every quarter of an hour for the first hour and every half hour after that. Six such observations were usually sufficient, and I was thus able to draw up charts which served for comparison in different cases.

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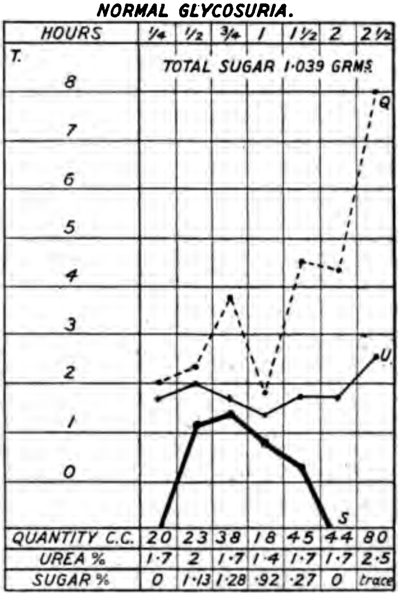
* In physiological experiments changes have been observed in the cells of the renal epithelium after prolonged administration of phloridzin. The doses used for this test in the human subject are minute, and the drug may be safely given in much greater quantity. No ill effects have followed doses of 10 grammes by mouth or of the subcutaneous injection of 2 grammes daily for a month (von Mering).

The estimations were made by the usual quantitative methods for the estimation of sugar. In order to obtain a sufficient quantity of urine for the estimation it was frequently necessary, unless a polyuria was already in progress, to give a diuretic. For this purpose I have used hot Contrexéville water or tea, and recently theocin (6 grains in cachets). The diuretic should be administered one half or three quarters of an hour before the commencement of the test, for the increased flow of urine does not commence for an hour or sometimes even two hours after the diuretic has been taken.

In Chart 20 the normal course of the elimination of sugar (S) after injection of 5 milligrammes of phloridzin is shewn, and the curves of urea (U) and quantity of urine (Q) also appear.



HOURS	¼	½	¾	1	1½	2	2½
QUANTITY C.C.	20	23	38	18	45	44	80
UREA %	1·7	2	1·7	1·4	1·7	1·7	2·5
SUGAR %	0	1·13	1·28	·92	·27	0	trace

Chart 20.—Normal glycosuria after injection of 5 mgr. of phloridzin. Observations made every quarter of an hour for one hour, then every half hour. S indicates the course of the glycosuria, U the course of urea excretion, and Q the quantity of urine.

Variation in the phloridzin glycosuria of normal kidneys.—It has been shewn by various observers that certain drugs diminish the secretion of sugar. Among these are glycerine, salicylate of soda,* jambul,† antipyrin,‡ and piperazin.§ There may be delay in the appearance of sugar in the urine. According to Albarran,* "variations in this are so great in different cases that it is difficult to distinguish any general rule, and we cannot attach great importance to the time at which the sugar begins to appear in the urine."

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* Coolen, *Archiv de pharmacodyn*, 1896, T. iii., p. 225.

† Hildebrandt, *Virchow's Archiv*, 1893, B. xxxi., S. 26.

‡ Sée and Gley, *Comptes rendus des séances de l'Acad. de Sc.*, 1889, p. 84.

§ Hildebrandt, *Berl. klin. Woch.*, 1894, S. 142.

My observations do not, however, coincide with this view, for the commencement of elimination in healthy individuals occurred, almost without exception, between a quarter and half an hour after the injection. When a delay occurred there was some interference with the renal function.

The normal duration of the glycosuria following an injection of 5 milligrammes of phloridzin is from two to three hours. It may exceptionally be prolonged as slight traces in the urine for five or six hours in a healthy individual.

The total quantity of sugar eliminated varies from 1 to 2 grammes. The lowest limit of normal glycosuria lies between 50 centigrammes and 1 gramme, and the highest between 2 and 2.50 grammes. Achard and Delamere† have shewn that a diminution of the quantity of sugar eliminated (hypoglycosuria), or an excessive diabetes (hyperglycosuria) may sometimes be observed without other proof of anatomical changes being present in the kidneys. Normal hypoglycosuria is less common than hyperglycosuria. These authors relate the case of a young girl who suffered from acute articular rheumatism accompanied by a slight albuminuria, in whom a complete absence of phloridzin diabetes was observed. The albuminuria disappeared, and the test was repeated, with the result that a normal glycosuria was obtained. The absence of glycosuria in this case was ascribed to a transient depression of renal function due to the elimination of poisons.

A similar absence of glycosuria has been observed in other maladies, such as catarrhal jaundice, alcoholism, and arterio-sclerosis, and Cloupet* observed hypoglycosuria in three cases of epilepsy where the kidneys were apparently healthy.

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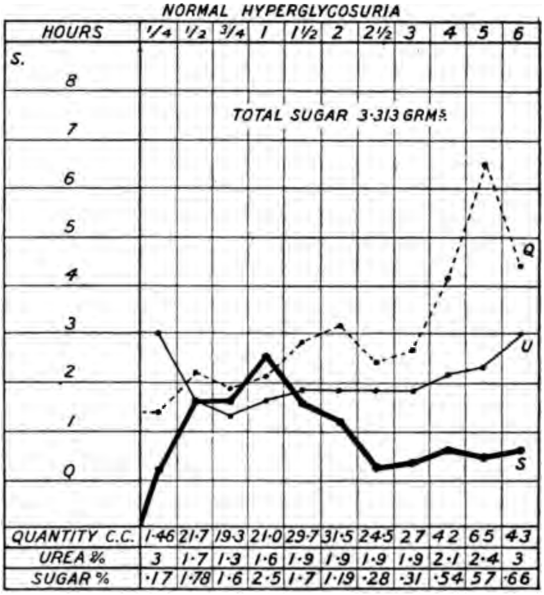
* "Exploration des fonctions rénales," 1905, p. 168.

† *Loc. cit.*

Normal hyperglycosuria is more frequently observed in healthy individuals than is a diminished elimination.



HOURS	1/4	1/2	3/4	1	1½	2	2½	3	4	5	6
QUANTITY C.C.	1·46	21·7	19·3	21·0	29·7	31·5	24·5	27	42	65	43
UREA %	3	1·7	1·3	1·6	1·9	1·9	1·9	1·9	2·1	2·4	3
SUGAR %	·17	1·78	1·6	2·5	1·7	1·19	·28	·31	·54	57	·66

Chart 21.—Normal hyperglycosuria after injection of 5 mgr. phloridzin in a healthy individual. Q indicates the quantity of urine, U the percentage of urea, and S the percentage of sugar.

Chart 21 shews an excessive production of sugar after the injection of 5 milligrammes of phloridzin in a healthy individual. The total quantity of sugar eliminated was 3.313 grammes. The elimination commenced 15 minutes after the injection, reached its maximum in one hour, and, after 2½ hours, persisted in traces till 6 hours after the injection.

Hyperglycosuria has also been observed under the most varying conditions, as in patients suffering from bronchopneumonia, typhoid fever, acute articular rheumatism, bronchitis, arterio-sclerosis, emphysema, cancer of the larynx, chronic rheumatism, and alcoholism.

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* Thèse de Toulouse, 1899.

The phloridzin test in renal disease.—1. Occasionally a *normal elimination of sugar* may take place when a renal lesion is present. In the literature of the subject a few such cases may be found. Among Delamere's cases * is one of tuberculous nephritis of the right kidney in a man of 53 years where 1.550 grammes of sugar were eliminated. In another case, in which an acute exacerbation had supervened on chronic nephritis, the excretion of sugar was 1.22 grammes; but on a subsequent trial it was 0.142 gramme. In a case of nephritis of pregnancy Miorcec† found a normal glycosuria.

Some of Jouffray's cases ‡ also gave a normal elimination of sugar. One case of old-standing nephritis in a woman of 50 years, a case of albuminuria complicating pulmonary tuberculosis, a case of albuminuria with diabetes insipidus, and one of gouty nephritis gave normal quantities of sugar after injection of phloridzin.

2. In almost all cases of pronounced renal lesion, and especially where the disease is bilateral, there is some variation in the phloridzin glycosuria. Usually this takes the form of *diminution* in the quantity eliminated, sometimes of *complete absence of sugar.*

Delamere has recorded 49 cases where a hypoglycosuria accompanied albuminuria, when a renal lesion of varying intensity was present. An autopsy was obtained in 16 of these cases. Pugnot and Revilliod§ have recorded similar observations in 21 patients suffering from renal disease.

Albarran has seen several cases in which a marked hypoglycosuria was present with insignificant lesions of the kidneys. Thus there was a diminished elimination of sugar in cases of movable kidney, slight pyelonephritis, and enlarged prostate, with no other signs of renal inefficiency. This observer also records instances of hypoglycosuria in unilateral renal lesions where the second kidney was functionally perfect by other tests.

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* Thèse de Paris, 1899.
† Thèse de Lyon, 1902.
‡ Thèse de Lyon, 1903.
§ *Archiv gén. de méd.*, 1902.

Among my cases was one of renal colic, in which the total glycosuria was only .53 gramme.

This patient (P. N., 477) was a man of 33, whom I saw at St. Peter's Hospital. He had suffered from pain in the left kidney for 6 months, and had several attacks of severe renal colic with pain shooting to the tip of the penis and frequent micturition, and on one occasion with pain down the left thigh. The left kidney was tender but not enlarged, and the bladder was healthy and the ureteric orifices normal. The urine was free from albumin, pus, and blood, but was said to have been thick at one time. I explored the left kidney without being aware that his temperature was up and rising. The examination of the kidney, renal pelvis, and ureter failed to reveal any abnormality. He subsequently developed and succumbed to purulent pericarditis and double empyema, the infection having originated in a carbuncle in his neck.

At the autopsy no cause for the renal colic was discovered nor could a lesion of the kidneys likely to cause diminution in the renal function be detected.

In another patient, a woman (E. W.) of 29 years, sent to me by Dr. John Lawrie of Woking, there was a movable kidney on the right side with an excursion ranging well below the umbilicus. There had been constant dull aching in the organ, and attacks of renal colic. An injection of 5 milligrammes of phloridzin produced only .614 gramme of sugar, which appeared in 15 minutes and continued for two hours.

In my cases of urinary obstruction there was diminished elimination of sugar, and when pronounced renal complications were present no sugar appeared in the urine.

Chart 22 shews the elimination of sugar in a man (W.) aged 50, who had complained of symptoms of stricture of the urethra for 4 years. The urine was turbid, 1016, acid, and varied in quantity from 25 to 30 ounces a day. The urea amounted to 1.9 per cent. There were no signs of renal disease. Elimination of sugar commenced an hour after the injection of 5 milligrammes of phloridzin and lasted 1½ hours. The total quantity eliminated was .361 gramme. Thus there was delayed, shortened, reduced elimination.

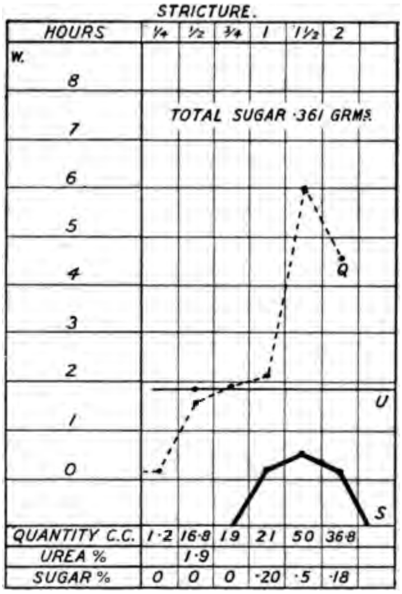


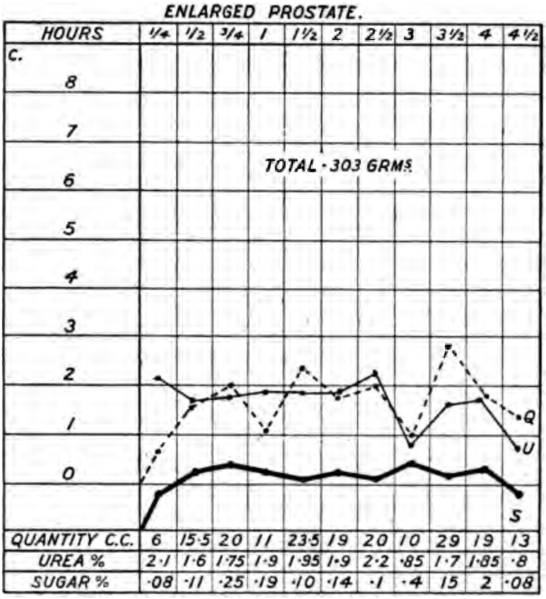
Chart 22. — Stricture of the urethra. Delayed, shortened, reduced elimination of sugar.

Another case (A. C.), a man aged 32, suffered from an impassable traumatic stricture of the bulbous urethra. He had fallen astride a plank and suffered from slight urethral hæmorrhage, and 4 months later was admitted to St. Peter's Hospital with an overdistended bladder and dribbling urine. There were no signs of renal disease. He passed 48 ounces of acid urine of 1008 density, containing a trace of albumin and .6 per cent. of urea.

Injection of 5 milligrammes of phloridzin produced .47 gramme of sugar, the commencement of elimination being delayed for ¾ hour. This case is of peculiar interest, for the patient later developed a large pyonephrosis, and the further investigation of his renal function will be described later (page 143).

Chart 23 shews the elimination of sugar in a case of enlarged prostate with interstitial nephritis of a moderate degree. The notes of the case are briefly as follows :—Mr. C., aged 67, was sent to me by Dr. Gurney Thompson, of Tottenham, suffering from symptoms of enlarged prostate. A dry, red, glazed tongue and marked thirst were the only symptoms of renal inefficiency. The urine was acid and contained a small quantity of pus and blood with some coarsely granular tube casts and bacteria. The density was 1015 and the urea amounted to 1.75 per cent. An injection of 5 milligrammes of phloridzin was followed by the appearance of traces of sugar in 15 minutes. The sugar continued to pass for 4½ hours, but the total quantity only reached .303 gramme. The glycosuria was thus prolonged and diminished. After suprapubic prostatectomy the patient was drowsy and apathetic with a dry, glazed

ENLARGED PROSTATE.



HOURS	¼	½	¾	1	1½	2	2½	3	3½	4	4½
QUANTITY C.C.	6	15·5	20	11	23·5	19	20	10	29	19	13
UREA %	2·1	1·6	1·75	1·9	1·95	1·9	2·2	·85	1·7	1·85	·8
SUGAR %	·08	·11	·25	·19	·10	·14	·1	·4	15	2	·08

Chart 23.—Prolonged, diminished phloridzin glycosuria (S) in enlarged prostate.

tongue, and absence of appetite for three days, but he then improved and made an uneventful recovery.

In another case of enlarged prostate (H. B., aged 68) with distended bladder and overflow of urine, there were symptoms of renal failure, namely bilateral renal pain, frontal headache, dry harsh skin, constant burning thirst, faint œdema of the abdominal wall, and copious aseptic polyuria. An injection of 5 milligrammes of phloridzin produced .57 gramme of sugar, and an injection of methylene blue failed to colour the urine. The patient was refused operation.

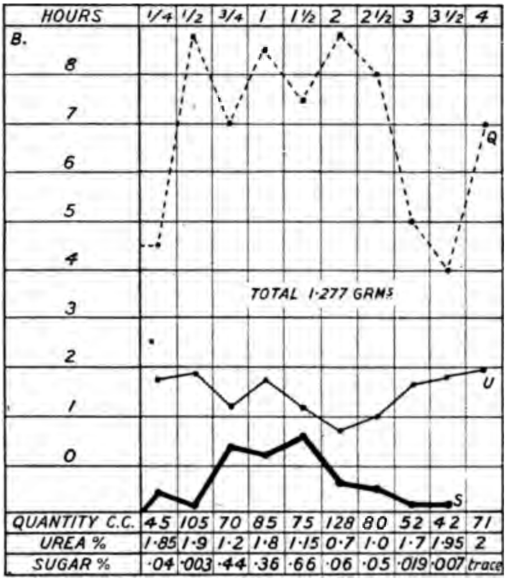
I have already referred (page 116) to a case of enlarged prostate (C. S.) in considering the methylene blue test. The patient shewed no signs of renal inefficiency, with the exception of a moderate polyuria, and the total urea output was well up to normal. No glycosuria followed the administration of phloridzin. The patient died of suppression of urine after prostatectomy, and the kidneys shewed advanced interstitial changes, and were hollowed from pressure.

In a case of oliguria which became anuria from obstruction to the ureters by a malignant growth in the bladder (*see* page 7), sugar failed to appear in the urine.

In cases of surgical diseases of the kidneys where the diseases originated in these organs, the elimination of sugar was diminished or there was complete absence of glycosuria.

In a case of movable kidney (E. W.) of moderate excursion and undamaged substance, with constant aching and occasional attacks of colic, .614 gramme of sugar passed in the urine after injection of 5 milligrammes of phloridzin. In another case of similar type (Mrs. D.) 1.308 grammes were passed. But in a woman of 50 (Mrs. B.) sent to me by Dr. Ross Sinclair of Parsons Green, where a large hydronephrosis of the right kidney had resulted from kinking of the ureter in a movable kidney, only .0375 gramme of sugar was estimated in this test. The condition was relieved by nephropexy.

There were two cases of single kidney, one remaining after nephrectomy for tuberculosis of the kidney and the other after nephrectomy for pyonephrosis complicating stricture of the urethra.


SINGLE KIDNEY.

HOURS	1/4	1/2	3/4	1	1½	2	2½	3	3½	4
QUANTITY C.C.	45	105	70	85	75	128	80	52	42	71
UREA %	1·85	1·9	1·2	1·8	1·15	0·7	1·0	1·7	1·95	2
SUGAR %	·04	·003	·44	·36	·66	·06	·05	·019	·007	trace

Chart 24.—Normal phloridzin glycosuria after nephrectomy.

In the case of nephrectomy for tuberculous disease (C. B., aged 41, sent by Dr. Oliver Kerr, of Camberwell), I had removed the kidney 18 months previously, after ascertaining that the urine of the second kidney was healthy. The patient eliminated 1.277 grammes of phloridzin from his solitary organ (Chart 24). He was in robust health. The second case (R., aged 57) has already been referred to in discussing the methylene blue test (page 116). After nephrotomy, the blue test was negative, and after nephrectomy it was positive, but considerably modified. The patient shewed pronounced symptoms of renal failure after each operation. I tested his renal activity with phloridzin some months after removing the kidney, and no trace of sugar appeared in the urine (Chart 25).

In two patients (T. and C. L.) for whom I removed aseptic calculi from the renal pelvis of one side, the sugar excretion was 1.82 grammes and 1.59 grammes respectively.

In another patient (J. R. H., aged 44), whom I saw in consultation with Dr. F. W. Collinson, of Preston, there was evidence of calculi in the left renal pelvis, the urine was foul, and a moderate degree of hydronephrosis was present in the left kidney. Injection of 5 milligrammes of phloridzin produced .510 gramme of sugar. I removed three small calculi from the dilated pelvis, and there was an uneventful recovery.

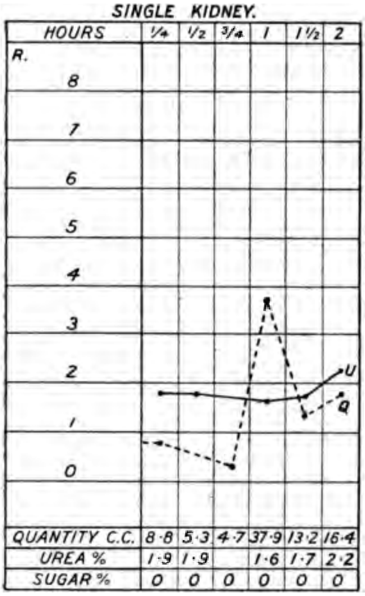


Chart 25.—Absence of phloridzin glycosuria in solitary diseased kidney after nephrectomy for pyonephrosis.

J. F. (*see* page 11) was the subject of advanced acute septic pyelonephritis, most marked on the right side. On May 9th, 1907, he had bouts of hiccough at a few seconds' interval, and was drowsy and partly conscious, with a temperature of 101.6, and was passing a small quantity of urine. Injection of 5 milligrammes of phloridzin failed to produce glycosuria. After nephrotomy on May 11th, the symptoms disappeared, and the test was again applied on June 3rd, but was again negative. The patient eventually recovered, and successfully underwent a perineal prostatectomy for malignant prostate.

The case of A. C., aged 32, has already been referred to on page 138. He suffered from impassable traumatic stricture, and secreted .47 gramme of sugar after injection of phloridzin. He was readmitted to St. Peter's Hospital six months later, with a large pyonephrosis on the right side. The urine was acid, 1013, contained albumin, and the urea was 2.5 per cent. in 42 ounces passed in 24 hours. The phloridzin test was reapplied, and no sugar could be detected in the urine. This patient survived nephrotomy, which relieved him of several pints of pus, but he refused nephrectomy, and left the hospital healed and in good health. When he left, no sign of the pyonephrosis could be detected, and the urine contained only a small quantity of pus.

3. In a few cases of urinary disease there was *increased elimination of sugar* or hyperglycosuria. In a girl of 18 years, whose left kidney I had recently removed for advanced tuberculous disease, there was still severe tuberculous cystitis. In this patient 5.21 grammes of sugar were rapidly eliminated, commencing half an hour after injection.

In a second patient (L. M.) there was chronic septic pyelonephritis, more marked on one side. There were periodical exacerbations and the general symptoms (wasting, drowsiness, dry, glazed tongue) pointed to a failing renal function. The patient passed 3.40 grammes of sugar in two hours. Right nephrotomy was performed, and the patient recovered and left the hospital well.

The value of the phloridzin test.—A diminished phloridzin glycosuria indicates a depressed renal function which is usually due to disease of the kidney, and a complete absence of sugar should be regarded as a sign of advanced renal lesion.

The elimination of a normal quantity of sugar by diseased kidneys has been occasionally noted in the literature, but this has not occurred with sufficient frequency to vitiate the test.

In slight lesions of the kidneys there is sometimes a tendency to exaggerate the significance of the lesion by an excessive reduction in the quantity of sugar eliminated. The test in these cases is too delicate, and, if unsupported by other evidence, might lead to erroneous conclusions. In the cases of unexplained renal colic and of movable kidney that I have quoted, this tendency to exaggeration was observed. But the test gave accurate evidence of the state of the renal function in most cases of urinary obstruction, and in the examples of renal disease the results were reliable. The presence of sepsis apparently influenced the elimination of sugar adversely in some of these cases.

Sugar failed to appear in the following cases :—

(1) Two cases of enlarged prostate with renal complications.

(2) One case of bilateral ureteral obstruction by malignant growth.

(3) Two cases of urethral stricture with pyonephrosis.

(4) One case of pyelonephritis.

In the cases of enlarged prostate and renal complications there were symptoms of renal disease in one, and none in the other. Both were submitted to operation, and the patient without renal symptoms died of renal failure. The obstructive oliguria case shewed no symptoms of renal failure apart from the scanty urine at the time of the test. There were well-marked symptoms of renal inadequacy in both the cases of stricture pyonephrosis, and also in the case of pyelonephritis.

The elimination of sugar followed what was known to be an improvement in the condition of two of these patients, for it appeared in the urine on a second test being made after recovery from operation.

Compared with the urea output and the general symptoms of renal inadequacy the phloridzin test was more delicate in my cases. The fallacy to which it was specially open was the pronounced effect which minor renal changes produced upon the glycosuria. It is possible that this fallacy may be overcome by the use of larger doses of phloridzin.

PART II

ESTIMATION OF THE FUNCTION OF ONE KIDNEY

CHAPTER

METHODS OF DIAGNOSIS DEPENDING UPON CLINICAL EXAMINATION, STATISTICS AND PATHOLOGY

Symptoms of Renal Failure—Local Signs of Disease—Absence of General and Local Symptoms—Statistics of Bilateral Renal Disease—Application of Statistics—Malformations of Genital System—Collected Cases of Anuria following Operation

In the foregoing chapters I have discussed the methods by which the combined function of the two kidneys may be estimated, and have indicated the type of case in which such observations are useful and necessary. I shall now pass to consider the means at the disposal of the surgeon of estimating the function of one kidney.

When one kidney is diseased, and it is accepted that its function is seriously impaired or totally destroyed, the question of prognosis, and the decision in regard to surgical interference and its extent, will in a considerable majority of cases depend upon the view which is taken in regard to the functional activity of the second kidney.

I shall briefly review the methods upon which, until a recent date, the surgeon had to rely for the data whereon to base his judgment in this matter.

1. Where one kidney is obviously diseased, the patient may show **symptoms of failure of the renal function,** and thus betray the reduced activity of the second kidney. These symptoms differ in no way from those which herald the failure of the renal function in diseases of the lower

urinary tract, and which have already been discussed (page 5 *et seq.*).

Briefly set out, they comprise headache, dry tongue, thirst, loss of appetite, and nausea, loss of flesh, a dry, harsh skin, and in the more advanced stages, emaciation, subnormal temperature, hiccough, vomiting, apathy, drowsiness passing into coma.

With these symptoms before him, the surgeon will be able to decide whether he will take the risk of advising surgical interference, and how far this may be carried.

2. But it is in the case where general symptoms of renal failure are absent that more information is required in regard to the functional power of the second kidney. The surgeon has relied upon the presence of **local signs of disease in the second kidney** for his judgment as to its function.

There may be enlargement, pain, and tenderness of the second organ, but these do not give unquestionable proof that the kidney is seriously diseased.

The remaining organ, when one kidney has not developed, or has been destroyed by disease or accident, or removed by operation, undergoes compensatory hypertrophy. This hypertrophy, according to Tuffier,* is more marked when nephrectomy has been performed than when it results from disease, but it is a constant feature in either case, and may lead to an enlargement of the organ to as much as twice the original size. Such an enlargement is a source of difficulty in diagnosis, the more so; that the kidney may be tender and ache without being actually diseased. Where tuberculous or calculous disease which has produced no symptoms has destroyed the other kidney, the enlarged, aching, hypertrophied organ is the one which is most likely to attract the attention of the surgeon, and to be the object of exploration, or even of nephrectomy.

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* "Études expérimentales sur la chirurgie du rein," Paris, 1889.

This is the more probable where the hypertrophied kidney is also the seat of disease, although less advanced than that of its neighbour.

In a case (a woman aged 25) recorded by Pinner,* there was a large tender left kidney, and the right kidney was not palpable, tender, or painful. The urine was cloudy, and contained tubercle bacilli. The large left kidney was removed, and the operation was followed by anuria and death on the fifth day. The kidney removed contained several abscesses in the lower pole and miliary tubercle of the rest of its substance, and was much hypertrophied. *Post-mortem*, the right kidney was not enlarged, but was completely transformed into a series of cavities filled with caseous pus.

Nor is the presence of a healthy kidney proved by the palpation of an organ apparently normal in size and insensitive. In a case recorded by Sendler† there was a tumour of the right kidney, and the left kidney was palpable, in good position, and not enlarged or tender. The right kidney was removed, and uræmia followed. An autopsy discovered a thin-walled cyst in place of the left kidney.

Aching and even some tenderness are not uncommon in a remaining healthy kidney after nephrectomy, during the time when hypertrophy may be supposed to be in progress.‡ I have noticed it especially in tuberculous cases. But the most severe pain I have met with was in a man (J. V., aged 44) who had his kidney explored and later removed by another surgeon, and subsequently came under my care. He gave a history of acute nephritis, which was treated in a hospital 9 years before. The kidney had been explored on account of severe pain, and removed for septic inflammation. Before nephrectomy he had not

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* *Archiv f. klin. Chir.*, B. lvi., 1898.

† *München med. Woch.*, 1899, S. 539.

‡ Tuffier (*loc. cit.*), from his experiments on animals, concluded that hypertrophy was complete in from 10 to 15 days, but this time is probably much exceeded in the human subject.

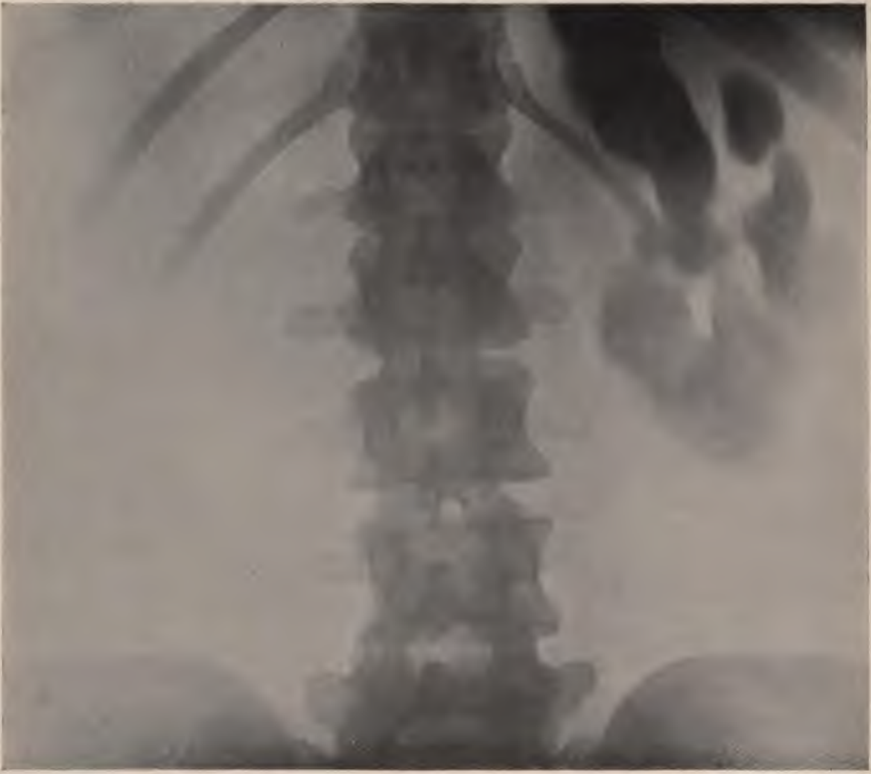

Plate V.—Skiagram of calculi in right kidney, and clear field in left kidney area. Nephrectomy; recovery; author's case. Skiagram by Dr. R. Morton. For illustration of kidney after removal, *see* Frontispiece. For analysis of urine of each kidney, *see* Chart 29 and page 246.

felt pain in the other kidney, but three weeks after the operation constant aching began in the remaining organ, and continued for about twelve months, during which time his urine was absolutely clear. There was, however, no tenderness, and I could never feel the organ.

The X-rays may give valuable aid in some cases of calculous disease. Extensive shadows in the second kidney may indicate that the margin of renal tissue is too small to maintain the function. On the other hand, the absence of shadows will prove that calculi are not present in the second kidney.

In the accompanying skiagram (Plate V.) large masses of calculi are seen in the right kidney, and a clear field in the area of the left. It was inferred from this that the right kidney was practically destroyed, and that the left was free from calculus, which is the most frequent form of disease of the second kidney where one is the seat of stone. It was proved by other methods that the second kidney was present and functionally healthy, and that the right kidney retained considerable functional activity. The right kidney as it appeared after nephrectomy is shewn in the *frontispiece*. The case (Mrs. J.) is described on page 238.

3. But the foregoing types form only a small number of the cases that are presented for consideration. The real difficulty arises when there are **no general symptoms of renal failure and no local signs of disease of the second kidney,** and these form the great majority of cases of surgical diseases of the kidneys.

It may be said that when extensive disease is diagnosed in one kidney the second must be sound or sufficiently healthy to carry on the function of the two if no symptoms of renal failure are observed. This conclusion is based upon the assumption that when widespread disease is recognised in one kidney it is to be accepted that its function is destroyed or so far reduced as to form a negligible fraction of the total function. But it is surprising how much active renal tissue may be found in a kidney the seat of massive calculous formation (see *frontispiece*) which is palpable as a large tender mass and even visible on the surface of the abdomen; or how much functional power may be retained in the apparently fibrous wall of a hydronephrosis. The active renal tissue, scarcely recognisable to the naked eye, which is distributed between the cysts of a congenital cystic kidney may be a considerable asset in the limited renal function of a case of bilateral cystic disease.*

Again, the absence of local signs of disease of the second kidney is no proof that it is healthy or even that a second kidney exists. Among 95 cases of post-operative anuria that I collected from the literature there were 10 cases of nephrectomy and nephrotomy where no second kidney was present. In these cases there were neither general symptoms of renal failure nor local signs of the absence of the kidney before the operation was undertaken.

There are some cases where "complete plugging of one ureter is known to have occurred by the alteration in the symptoms during the course of the disease,"† and yet the urine continues to be excreted. The urine passed from the bladder must come from the second kidney. The urine passed by the urethra in cases of renal fistula with free draining of urine may also be looked upon as coming from the second kidney. But these are exceptional cases; as a rule no such convincing evidence of the presence of a functional second kidney is provided.

4. The **statistics** that have been compiled with regard

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* Köster first shewed that in contracted kidneys, the portions of the kidneys that remained intact underwent compensatory hypertrophy. Thovel (*Virchow's Archiv*, vol. cxlvi., 297, 330) has demonstrated a similar change at the margins of an infarct of the kidney, while Guyon and Albarran (Assoc. franc. d'urologie, 1897) found evidence of compensatory hypertrophy in the wall of hydronephrotic sacs, and Albarran (*La presse méd.*, Feb. 22, 1899) recognised hypertrophy in the remaining portion of a kidney containing a malignant growth.

† Morris, "Surgical Diseases of the Kidney and Ureter," 1901.

to the bilateral incidence of various renal disorders may be used to aid in the diagnosis of the condition of the second kidney.

(1) **Single and atrophied kidneys.**—The most important statistics are those compiled by Morris,[*] from the *post-mortem* records of Guy's, Middlesex, St. Bartholomew's Hospitals, and Great Ormond Street Hospital for Sick Children. A total of 15,904 examinations revealed 6 cases of "absence or extreme atrophy" of one kidney (1 in 2,650), and 59 "atrophied kidneys were found in 8,178 inspections."

Weir[†] stated the number of single kidneys at 1 in 5,000, and Peterson[‡] at 1 in 1,500, a considerable difference; but Morris, by adding these two sets of figures, gets 1 in 3,250, a figure not differing greatly from his own statistics.

Various collections of cases of solitary and shrunken kidneys have been made.

Beumer[§] described 48 cases in the literature up to 1878, Ballowitz[||] carried these on to 1895 and totalled 213 cases, and Mankiewicz[¶] continued the collection to 1900 and brought the number up to 234 cases.

In recent years the number of cases of solitary kidney recorded have greatly multiplied, and reports of such cases are so common as to lead to the suspicion that the statistics quoted fall considerably below the actual number.

(2) **New growths of the kidney.**—Bilateral malignant tumours of the kidney, apart from secondary deposits, are almost, if not entirely, confined to sarcoma occurring in children. In these they were bilateral in—

7 out of 72 cases (Guillet[**])
5 out of 59 cases (Ebstein[††])

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[*] "Surgical Diseases of the Kidney and Ureter," 1901.
[†] *New York Med. Jour.*, Dec. 27, 1884.
[‡] *Medical Times and Gaz.*, Oct. 7, 1882.
[§] *Virchow's Archiv*, B. lxxii., 1878.
[||] *Virchow's Archiv*, B. cxli., 1895.
[¶] *Monatsber. ü. d. Gesammtleistungen u. d. Gebiete d. Krankh. d. Harn u. Sex. Apparat.*, v., 1900.
[**] Thèse de Paris, 1888.
[††] Ziemssen's Cyclopædia of Medicine, 1877, vol. xv.

12 out of 118 cases (Kelynack*)
2 out of 50 cases (Leibert†).

Adding these together we get 26 in 299 cases, or 1 in 11.5.

(3) **Polycystic kidney.**—The personal cases of Israel‡ and Morris§ are interesting. The former surgeon records 4 cases, all of which were bilateral, while the latter saw 7 cases, only 3 of which were bilateral.

The collected statistics refer to cases occurring in adult life. The disease in infants is almost invariably bilateral.

Both kidneys were affected in—

150 out of 191 cases (Küster||)
25 out of 26 cases (Dickinson¶)
65 out of 66 cases (Lejars**).

(4) **Calculous disease of the kidney.**—The pathologist and the surgeon are at variance concerning the frequency with which calculous disease affects both kidneys. The former places the number of bilateral cases high, while the latter looks upon renal calculus as pre-eminently a unilateral disease. That both are in part correct in their estimate is shewn by numerous carefully compiled series of statistics. Cases of renal calculus, with their distressing train of symptoms, are usually brought under the notice of the surgeon at a time when one kidney is affected, or when the symptoms and history point to a unilateral affection. Calculous disease affecting the kidney and left undisturbed eventually leads to deposit in and destruction of both organs, and the pathologist meets with these cases in greater proportion. The discrepancy in the figures which follow is thus explained.

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* "Renal Growths," 1898.

† *Jahrb. f. Kinderheilk.*, xxi., 1884, p. 276.

‡ "Nierenkrankheiten," 1901.

§ *Loc. cit.*

|| "Chirurgie der Nieren," 1902.

¶ "On Renal and Urinary Affections," 1885.

** "Du gros rein polycystique de l'adulte," Paris, 1888.

38 in 76 cases, 50 per cent. (Legueu*)
50 per cent. (Tuffier†)
27 per cent. (Israel‡)
21 in 83 cases, 25.3 per cent. (Torrès§)
90 in 764 cases, 11.78 per cent. (Küster||)
10 per cent. (Morris¶).

(5) **Suppurative pyelonephritis.**—The most frequent form of diffuse suppurative pyelonephritis is that which follows upon the upward spread of septic inflammation from the bladder. These cases represent the last phase of most obstructive and inflammatory diseases of the lower urinary tract. In the final stages they are almost without exception, bilateral, but at an earlier time they are frequently unilateral, or at least the disease on one side is much more advanced than that on the other. There are few available statistics.

The disease was bilateral in about 50 per cent. (Küster**).
59 in 71 cases, 83 per cent. (Weir††)
19 in 130 cases, 86 per cent. (Goodhart‡‡).

(6) **Tuberculous disease of the kidney.**—The statistics given by surgeons differ from those of pathologists in regard to the frequency with which the disease is found to have affected both kidneys. The insidious progress of tuberculous disease of the kidney is, however, one of the special features of these cases, and it is not rare to find that when the patient seeks surgical aid both kidneys are already affected, although to a different degree. Thus, when the cases of death from uræmia or anuria following surgical operation upon one kidney are considered (p. 157), it will be found that a large proportion (29.4 per cent.) of these cases were tuberculous in nature, and that the destruction of the

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* Thèse de Paris, 1891.
† "Traité de Chirurgie," 1899, T. vii.
‡ "Nierenkrankheiten," 1901.
§ "Des calculs du rein et de la nephrotomie," Thèse de Paris, 1878.
|| "Chirurgie der Nieren," 1902.
¶ "Surgical Diseases of the Kidneys and Ureter," 1901.
** *Loc. cit.*
†† *Med. News*, 1884, Dec.
‡‡ *Guy's Hospital Reports*, xix., 1864.

second kidney by the tuberculous disease was the cause of death.

Of 27 operation cases 8.3 per cent. were bilateral (Israel*).

Of 88 cases 9 per cent. were bilateral (Facklam†).

Of 61 cases 17 bilateral, 27.8 per cent. (Fischer‡).

Of 100 cases 17 bilateral (Vigneron§).

Of 32 cases 19 bilateral, 59.3 per cent. (Bright||).

Of 81 cases 38 bilateral, 46.9 per cent. (Heilberg and Oppenheimer¶).

Of 205 cases 99 bilateral, 48 per cent. (Palet**).

Of 95 cases 47 bilateral, 49.4 per cent. (Dickinson††).

Non-operated cases 51 per cent. bilateral (Vigneron).

When we use these statistics in the diagnosis of an individual case their value is somewhat restricted. On referring to the figures, it will be seen that malignant growths of the kidney are unilateral in 9 out of 10 cases, and this is accepted as a guarantee that in removing a kidney containing a renal growth little risk is run of the patient having submitted to a useless operation from the presence of a second tumour in the remaining kidney.

Again, it is known that the ratio of solitary kidneys is 1 in 2,650 cases, and that a kidney may be removed with but small risk of the patient being dead of uræmia in a few days, from the removal of his entire urine secreting tissue.

These facts are so well known that the question of the presence or health of a second kidney in such cases may never be considered. But even the apparently remote chance of the nephrectomy of a solitary kidney

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* *Deut. med. Woch.*, 1890, No. 31, "Nierenkrankheiten," 1901.

† *Archiv f. klin. Chir.*, B. xlv., S. 714.

‡ Thèse de Paris, 1892.

§ *Annales d. malad. d. org. génito-urin.*, Ann. 11, No. 9. Thèse de Paris, 1892.

|| Quoted by Senator, "Nierenkrankheiten," 1896.

¶ Quoted by Guterbock, "Krankheiten der Harnorgane," 1898.

** Thèse de Lyon, 1893.

†† "On Renal and Urinary Affections," 1885.

must be reckoned with in renal surgery, for the literature contains not a few instances in which this disaster has occurred, and there must be many others unrecorded. In 93 cases of death from uræmia or anuria setting in within the first few days after an operation upon one kidney that I collected from the literature, there was no second kidney in 10, and this organ was "completely atrophied" in 8.

5. It has long been recognised* that the congenital absence of a kidney may be accompanied by some **malformation in the genital system,** and if this is such as may be readily recognised, a hint as to the absence of the kidney may thus be obtained.

In the Ballowitz collection† of 213 cases of congenital defects of the kidneys, the state of the genital organs was mentioned in 103, and in 73 of these (70.8 per cent.) some malformation was present. Of these 28 were male and 41 female, the sex of the remaining 4 cases was not stated.

Further, the genital malformation is almost without exception on the same side as the renal defect. In only one of that large collection of cases does the malformation appear to have been on the side of the normal kidney.‡

Paltauf § has discussed the question from another point of view. In 79 cases where uterus bicornis was present 36 had also a defect of the urinary apparatus, and the kidney was always absent on the side of the horn of the uterus which was rudimentary.

The discovery of a maldevelopment of the genital organs has not always been taken as a hint of the absence of one kidney, and it has even led to the operation by which the solitary kidney was removed.

Two striking examples are on record. In a case described by Buss* a woman with hare lip and cleft palate suffered from severe pelvic pain each month, and absence of the menstrual flow. There was absence of the vagina and a swelling, supposed to be a collection of blood in front of the rectum. It was resolved to remove the ovaries. The left ovary was found and excised, and the swelling in Douglas's pouch removed and found to be a hypertrophied kidney. The patient died on the seventh day of uræmia. There was no right kidney or ureter, no uterus, no right ovary.

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* Beumer referred to the association of these deformities in his article on renal defects in 1878 (*Virchow's Archiv*, lxxii., 1878, S. 344), and it has been discussed by most writers on the subject since his time.

† *Virchow's Archiv*, cxli., 1895.

‡ Lombroso's case, *Gaz. Med. Italiana*, Feb., 1860; *L'union méd.*, Tome vi., Paris, 1860.

§ *Med. Jahrb. des k. k. Gesellsch. der Aerzte in Wien*, 1885.

In Polk's case† there was periodical pain in the left iliac fossa in a girl of 19. There was no vagina and no uterus, and in the left iliac fossa was a movable oval tumour. The tumour was removed and found to be a hypertrophied kidney. The patient died on the eleventh day of uræmia. No trace of a right kidney, ureter, or renal artery could be found, and there was no uterus, vagina, or clitoris, and the Fallopian tubes were rudimentary.

The value of this sign in the diagnosis of solitary kidney may be summed up as follows. Of the total number of cases where only one functional kidney exists congenital atrophy or want of development accounts for the absence of a second kidney in rather more than 10 per cent. (10 cases in 95 in my collection). Of this 10 per cent. from one-third to one-half shew some anomaly of the genital system. The genital malformation is most frequently found, is most extensive, and most readily recognised, in the female subject.

The methods that I have discussed in this chapter provide evidence in a certain number of cases upon which a reliable estimate of the function of the second kidney may be based. But there still remain a large number of cases where an operation is proposed upon one kidney, and in which no hint can be obtained of the presence or absence or of the health or disease of the second kidney.

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* *Zeitschr. f. klin. Med.*, B. xxxviii., H. 4, 5, 6.

† *N. Y. Med. Jour.*, Feb. 17, 1883.

I have collected from the literature 95 cases* of operation upon one kidney where anuria and uræmia commenced within the first few days after operation, and where apparently no suspicion was entertained before embarking upon the operation that the second kidney was not present and sufficiently healthy to maintain the renal function.

The *condition of the kidney operated upon* was as follows :—

Tuberculous disease	28
Calculous disease	25
Pyonephrosis	9
Hydronephrosis	6
Malignant disease	6
Suppurative pyelonephritis	5
Floating and displaced	5
Cystic	4
Hydatid cyst	1
Traumatic abscess	1
Nephritis	1
Fistula of the ureter	1
Healthy	1
Not stated	2
	95

In these, nephrectomy was performed in 65 cases, and nephrotomy or nephrolithotomy in 30.

In the 28 cases of tuberculous disease, the second kidney was the seat of tubercle in 13 and amyloid disease in 4. It was atrophied in 1, fatty in 1, cystic in 1, and shewed nephritis in 1. In 2 cases there was no second kidney, and in 5 no *post-mortem* examination was made.

In 25 cases of calculous disease there were calculi in the second kidney in 12. There was atrophy and degeneration in 4, and the remaining organ was the seat of fatty disease in 2, amyloid disease in 1, hydronephrosis in 2, and interstitial nephritis in 1; there was no autopsy in 3 cases.

In 9 cases of pyonephrosis the second kidney was the seat of pyonephrosis or suppurative pyelonephritis in 4,

* *See* Appendix.

parenchymatous nephritis in 1, cystic and waxy disease in 1, and hydronephrosis in 1. There was no examination in 2 cases.

In 6 cases of hydronephrosis the second kidney was the seat of hydronephrosis in 1 case, it was atrophic in 2, granular in 1, and the seat of parenchymatous nephritis in 1 case. There was no second kidney in 2 cases. In 6 cases of malignant disease of the kidney there were secondary nodules in the remaining organ in 2, and it was shrunken and cystic in 1, and hydronephrotic in another. No examination was made in two cases.

In 5 cases of suppurative pyelonephritis the second kidney was the seat of suppurative pyelonephritis in 2 and fatty degeneration in 2; while the condition of the organ was not stated in the remaining case.

The following list shews the *condition of the second kidney* in these cases of post-operative anuria:—

Tuberculous disease	14
Calculous disease	13
Absent	10
Atrophied and shrunken	8
Amyloid degeneration	6
Fatty degeneration	6
Hydronephrosis	5
Suppurative pyelonephritis and abscess	4
Interstitial nephritis	4
Parenchymatous nephritis	3
Pyonephrosis	2
Malignant disease	2
Polycystic disease	2
Cyst	1
No *post-mortem* examination, or unstated	15
	95

From these figures it will be seen that in cases of death from anuria and uræmia following operations upon kidneys, the seat of tuberculous or calculous disease or of pyonephrosis, the most frequent cause is the development of the same disease in the second kidney.

CHAPTER II

CYSTOSCOPIC EXAMINATION OF THE URETERIC OPENINGS

The Efflux—Absent Efflux—Copious Efflux—Murky Efflux—Purulent Efflux — Hæmorrhagic Efflux — Difficulties in Finding Ureteric Orifice—Absent or Displaced Orifice—Pathological Changes at the Orifice—Chromocystoscopy

THE discharge of urine or other material from the ureteric orifice might be expected to give valuable assistance in the investigation of renal disease, and this is the case when the localisation or diagnosis of an obscure disease is the subject of inquiry.

But when the diagnosis is already made, and the sole object of investigation is to measure the functional activity of the kidney, the information gained by the examination may be less convincing. I shall consider only such points as serve the purpose of the present investigation.

A.—THE EFFLUX

At rest the ureteric opening appears as a fine, short red line, situated near the outer end of the ridge which marks the base of the trigone. If this area be watched for some seconds the part of the ridge to the outer side of the ureter will be seen to swell, and the area around the ureteric opening is drawn outward, and at the same time the lips of the orifice become rigid and the ureteric meatus gapes. A jet of urine is then thrown into the medium with which the bladder is distended. Usually the swirl of the fluid can readily be seen, but if the jet is thrown sluggishly this may not be evident. It

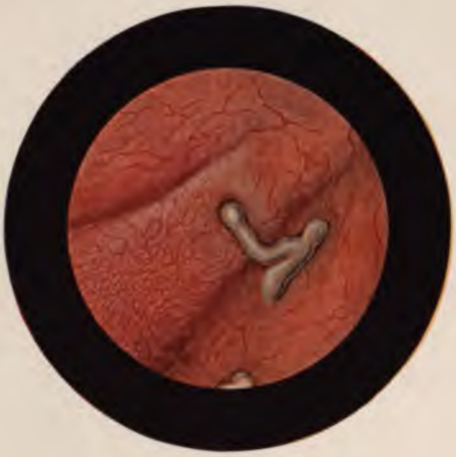
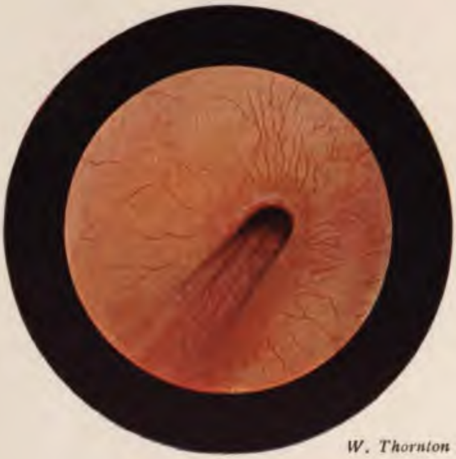


Fig. 1.



W. Thornton Shiells, del.

Fig. 2.

PLATE VI.

Fig. 1. Discharge of semi-solid pus from ureter.

Fig. 2. Dragged out ureter in tuberculous kidney.

(R. S., page 16), where the renal function was so poorly discharged that I refused operation, and the patient died of uræmia a few months later, large quantities of pale urine were passed, and both ureters were observed actively discharging the clear fluid.

The polyuria of advanced interstitial nephritis and of waxy disease may be observed on the side of the second kidney in renal surgery. Völcker and Joseph* noted a rapidly repeated efflux in compensatory hypertrophy of the kidney. Albarran † found that contraction of the mouth of the ureter was absent in dilatation of the ureter, and the discharge of urine was continuous.

3. A murky urine containing pus or *débris* momentarily fogs the cystoscopic view as it shoots from the ureter, and then the medium clears again as the cloud diffuses.

A urine which shews a distinct murky jet at the ureteric meatus on cystoscopic examination will appear much more opaque when collected in a glass jar.

The jet may be frequently repeated, pointing either to the presence of an irritant in the renal pelvis or ureter, or to the secretion of an increased quantity of urine. We may assume that the kidney on the side on which such an efflux is observed is producing at least an average quantity of urine to which pus or *débris* is added, but no indication is given as to the quality of the work performed by the kidney.

In cases of pyonephrosis where the ureter was patent Albarran observed a slow type of ureteric contraction. There were long pauses of 2 to 2½ minutes, followed by a voluminous efflux.

4. The expression of a worm of semi-solid waxy-looking pus from a ureter (Plate VI., Fig. 1) is a sign of grave import in estimating the value of the renal function. Here there is the production of a large quantity of thick pus

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* *Münch. med. Woch.*, 1903, 2028.

† "Exploration des fonctions rénales," 1905.

without the addition of sufficient urine to dilute or suspend it. In such a case, the ureteric opening is normal, or it may be circular and rigid and the edge reddened. A yellow point appears, and is slowly increased, and a yellow worm-like pipe of pus is extruded and slowly rolls down the side of the ureteral ridge into the post-trigonal depression, and lies there as a pellet of pus. After a minute or so this process is slowly repeated, but the interval is much longer than that between the jets of urine from a healthy kidney. I have notes of two such cases, and have a third under my care at the present time.

Mrs. P. was sent to me by Dr. Robert Purdie, in November, 1904, with a history of attacks of severe pain, at first in the left and later in the right side of the abdomen, at intervals for 8 years. The pain was usually started by exertion, and would last for a few days to a month. There was increased frequency of micturition, amounting to ten minutes during the day, and about fifteen minutes at night. The urine was acid and milky with pus. There were no signs of renal failure. The right kidney was enlarged and hard.

She postponed further examination for 18 months, when I saw her again (May, 1906). The pain had now almost disappeared, and only came on in the right side after exertion. For a month she had felt languid and ill, and had been vomiting. The urine was thick with pus.

There was a large mass in the right loin, extending forwards to the middle line and down into the right iliac fossa. With the patient lying on her back the tumour projected forwards as a visible swelling. The mass was hard, smooth, and tender. The frequency of micturition had subsided to four times during the day and four times at night.

With the cystoscope the bladder was slightly reddened. Masses of solid pus lay in the post-trigonal depression. The rim of the right ureter was reddened, and at intervals a solid worm of pus was slowly squeezed out. There was no fluid efflux. On June 14th I operated and removed a very large kidney distended with thick pus. Dense adhesions bound the kidney to the liver above and to the colon below. The operation was difficult and prolonged, and the patient much collapsed after it. She died of shock 10 hours later.

The excised kidney was converted into a series of large cavities which contained thick pus. Several calculi lay in the pelvis, and the walls of the cavities were tough, and were in a condition of chronic suppurative pyelonephritis.

In the second case (H.) there was a history of eleven years' symptoms of renal trouble, and the kidney contained much semi-solid pus and *débris* and calculi.

In the third case (J. H. V., sent to me by Dr. Howard Pirie) there had been pyuria for three years. The patient could remember slight pain in the left side. There was frequent micturition at times, and occasionally a streak of blood in the urine. He was under the care of a hospital surgeon for three weeks with a diagnosis of cystitis, and was circumcised and the bladder washed.

On cystoscopy the bladder was healthy except for a few small patches of subacute cystitis. The left ureter was larger than the right, and the lips were thick and reddened. My notes read as follows: "A stream of semi-solid pus passes at long intervals from the ureter down to the side of the trigone like a stream of lava, and small plugs of pus are scattered around."

The left kidney was difficult to feel on account of the contraction of the abdominal muscles. No shadow was detected in two X-ray examinations, and tubercle bacilli were not found in the urine.

I exposed the left kidney and found it small and firmly adherent to its surroundings. The tough adhesions gave some trouble in performing nephrectomy. After removal the organ was found to be small and tough. The pelvis contained several calculous-like masses, which were, however, found to be fragments of old blood-clot mingled with crystals. The whole substance of the kidney was converted into a tough pale grey tissue, resembling the infiltration which precedes caseation in a tuberculous kidney. On microscopical examination there was a uniform dense round-celled infiltration throughout the whole kidney tissue, but no giant cells or tubercle bacilli were discovered. The condition was one of chronic diffuse septic pyelonephritis.

5. A striking picture is produced by a jet of blood or of blood-stained urine issuing from the ureter, and is an important guide in the localisation of the hæmaturia to one or other kidney. But beyond demonstrating the presence of the kidney, no information is obtained as to the functional value of the organ.

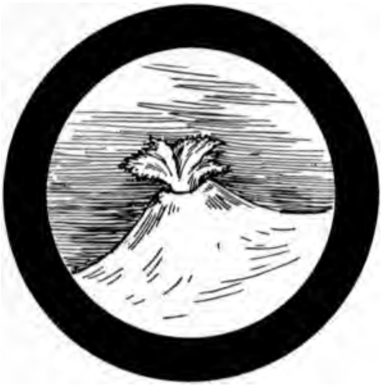

Fig. 6.—Irregular grey blood clot projecting from left ureter in case of hæmaturia.

Usually, however, where such a phenomenon is observed the kidney which is bleeding is the one which is to be operated upon, and no change is observed on the side of the second kidney.

6. I have never seen a "solid efflux" of blood and *débris* such as Mr. E. Hurry Fenwick describes,* but I have met with a case of hæmaturia in which an irregular greyish spongy-looking clot projected from the left ureter (Fig. 6). The bleeding had been copious, and was caused by a small stone in the left renal pelvis. The renal function was not seriously impaired.

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* "Ureteric Meatoscopy in Obscure Diseases of the Kidneys," 1903.

B.—THE URETERIC ORIFICE

The orifice of the ureter is found cystoscopically by turning the beak of the instrument downwards, so that the window looks upon the trigone. The base of the trigone will usually be seen as a low transverse ridge, and the instrument is rotated so that the eye follows this ridge outwards to the right or left. At its outer ends the ridge sinks to the level of the bladder wall. The deeper colour of the trigone will also assist in distinguishing it from the pale pink of the general bladder surface. Set upon this ridge, and near its outer end, is the fine red streak of the ureteric opening.

1. **Fallacies and difficulties in the recognition of the ureteric orifice.**—There may be difficulty in recognising the opening. It may lie among the folds of mucous membrane of a reddened puffy trigone, or the interureteric bar may be lost amid the ridges of a trabeculated bladder and the ureter be unrecognisable among the slits and openings which lie between.

In an otherwise healthy bladder, a round split-pea sized opening with sharply-cut edges may appear just behind the outer end of the ureteric ridge, and sometimes an exactly similar opening may be observed symmetrically placed upon the other side of the bladder base. Sometimes the opening is a little higher up, but this is the usual place. These are the openings of small congenital diverticula which may be found in this position, and they should not be mistaken for the ureteric openings. If cystitis is present and there are flakes of muco-pus floating in the medium, the appearance is even more deceptive, for the respiratory movements, the motion of the approaching cystoscope beak, or the swirl of the urine from the neighbouring ureteric orifice, may make the shreds dance and circle, project them and draw them back as if a discharge of urine from the opening actually took place and the flakes were caught in its stream or eddies.

2. **Congenital malformation and malposition.**—The ureteric opening on one or other side may be absent, or it may lie in some unusual situation.

(*a*) When one ureteric opening is recognised as being absent by a competent cystoscopist, it must be inferred that the kidney on the same side is congenitally absent. In 213 cases of congenital absence of one kidney collected by Ballowitz, the ureter was absent in all but 15 cases. There is, I believe, only one case on record where a kidney was absent on one side, and a ureter arising from this side of the bladder passed across the middle line and served to drain the solitary kidney on the opposite side of the body.* With an absent ureteric orifice on one side there may sometimes be an arrest in the development of the corresponding half of the trigone muscle. This part of the bladder base will therefore appear flat, or the normal side may seem raised and hypertrophied by comparison. Five in 198 cases of absent ureter shewed a flattening of this part of the bladder (Ballowitz). It is particularly necessary here to remember the fallacy of small congenital pockets in the ureteric area such as I have referred to above.

When a solitary ureteric opening exists it is usually normally placed, but it may be displaced nearer to the middle line of the bladder (2 in 198 cases of absent ureter, Ballowitz).

Post-mortem records shew that one ureter may be absent from its natural position and open into the urethra, vas deferens, or elsewhere. These cases are of no clinical importance; they have been found in infants, and would have been unrecognisable had life been prolonged.

(*b*) The cystoscopic discovery of two ureteric orifices is not a guarantee that two kidneys are present.

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* Horand's case, *Soc. anat. de Par.*, April, 1905. *Annales des malad. d. organ. génito-urin.*, 1906, 24, ii., 1503. *Lyon méd.*, 1905, civ., 718, 721.

Out of 213 cases of the Ballowitz collection the semblance of a healthy ureteric orifice was present on the side of the absent kidney in 15.

In these cases a fibrous band of varying length represented the ureter, and this contained a lumen for some part of its course which communicated with the bladder. This condition might lead to the erroneous conclusion that two kidneys were present, were the examination confined to a cursory glance at the ureteric openings, but the absence of efflux confirmed by the methods that I shall later describe would lead to the diagnosis of an absent or functionless kidney.

In three cases there was merely a dimple in the position of the ureteric orifice. I have seen such a dimple alongside a normal ureter, and have demonstrated its shallowness with the point of a ureteric catheter. In one case under my care there were two apparently normal ureteral openings lying side by side at the right end of the ureteric bar and a single opening at the left end. In another case there was a double opening on the left side and a single one on the right. These cases merit a short notice.

C. M., aged 40, attended my out-patient department at St. Peter's Hospital in 1903, and again in 1905. On the first occasion he had renal colic on the left side, which disappeared without the passage of a stone, and in April and June, 1905, there were severe attacks of right renal colic lasting seven hours, accompanied by intense strangury, but no hæmaturia.

On cystoscopy the bladder mucous membrane was healthy. The right horn of the trigone was broader and slightly more prominent than the left, and lying alongside each other in the normal position of the ureteric opening were two healthy-looking ureteric orifices—an upper and a lower, or an anterior and a posterior. I examined these with the ureteric catheter in June and in November, 1905, and again in September, 1906. Professor Johnson Symington, of

Belfast, was present in November, and discussed the anatomical aspect of the case with me. The ureteric catheter passed with ease into the upper or posterior opening, and was pushed onwards along the ureter without hindrance. From this ureter urine was collected, and at the same time urine was seen issuing from the lower or anterior opening. I failed to catheterise both openings simultaneously. A catheter passed into the lower or anterior opening for three quarters of an inch was arrested at this point, and I could not coax it further. A puff of murky urine stained with blood shot out alongside the catheter point, and blood oozed out after the catheter was withdrawn. The X-rays failed to demonstrate a shadow. *Per rectum* both ureters were thick, and there was a suspicion that a buried nodule lay in the right ureter. The right kidney was not palpable or tender. There was probably a double ureter on the right side in this patient, and I believe that the lower duct contained a small calculus at its vesical end.

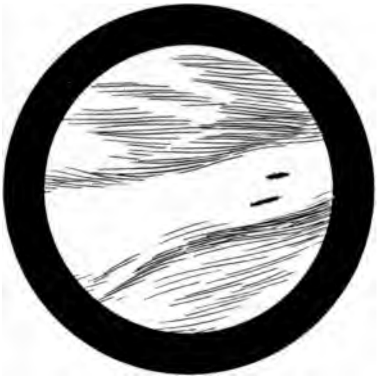
Fig. 7.—Double ureteric orifice on left side.

The second patient was a man (J. M., 265 v.), aged 40, who complained of frequent micturition of 3 years' duration. The urine was pale and clear and of low specific gravity, and the patient was intensely neurotic. On the left ureteric ridge there were two healthy ureteric orifices, both apparently emitting urine (Fig. 7). The right orifice was single and normally placed. I passed a ureteric bougie into each of the left orifices separately, and the bougie passed up the ureter without difficulty. I was unable, however, to pass a bougie along both simultaneously for the purposes of radiography, as the urethra was too narrow to admit of the larger instrument. It is difficult to say in this case whether a complete double ureter existed or whether the left ureter was bifid at its lower extremity.

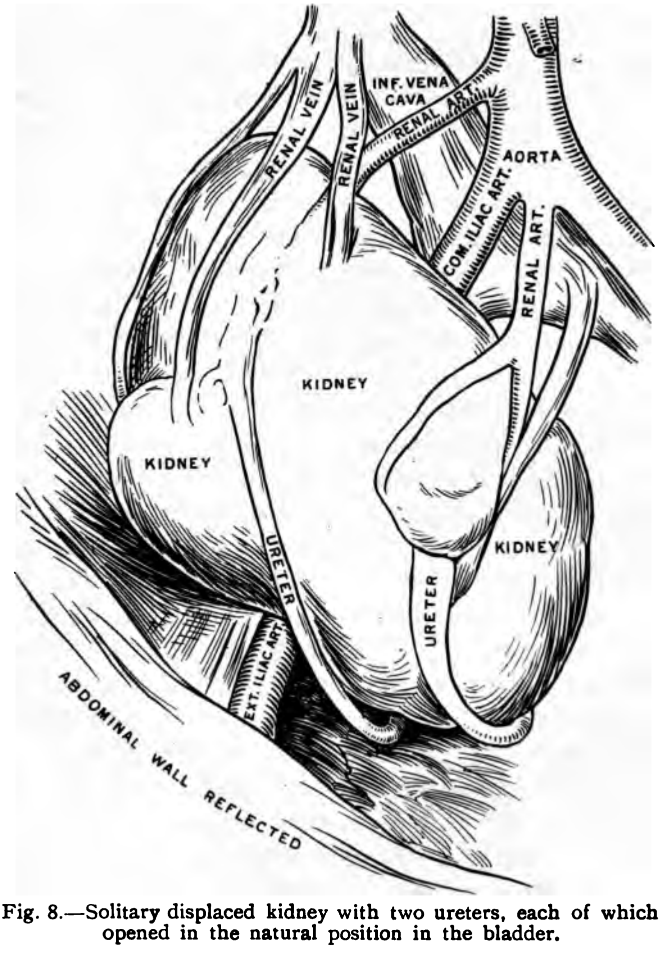

Fig. 8.—Solitary displaced kidney with two ureters, each of which opened in the natural position in the bladder.

I have already described a case of double ureter that I found *post-mortem* (page 28).

(*c*) A rare condition, but one which might lead to a serious and unavoidable mistake in diagnosis, is that in which two normally placed ureteric openings are present in the bladder, both emitting urine, but arising from a single kidney.

For the notes and an excellent photograph of the following case I am indebted to Professor Johnson Symington, of Belfast, who met with it in a dissection body (Fig. 8). I give the description in Dr. Symington's own words :—

"In a female subject, aged 19, there was no kidney on the left side. On the right side a kidney was situated in the right iliac fossa, and extended over the brim into the pelvis. Its upper end reached to the level of the intervertebral disc, between the third and fourth lumbar vertebræ. The lower portion, which dipped into the pelvis, was bent nearly to a right angle with the upper part, and extended down to the third sacral vertebra.

"The kidney mass was supplied by three renal arteries, one from the right side of the aorta, one from the right common iliac, and a third from the point where the middle sacral artery comes off. There were two ureters, which passed down to the bladder and opened into this viscus in the usual situations.

"Mr. A. Foulerton made a cystoscopic examination of the bladder and found the vesical orifices of the ureters in their normal position, but the right orifice was a little more elongated than the left, and the right portion of the interureteric bar was somewhat thicker than the left. There was nothing in the cystoscopic examination to lead one to suspect the abnormal condition of the kidneys."

These conditions may briefly be summarised as follows :—

i. When the ureteric opening is absent on one side the kidney on that side is also absent.

ii. The observation of two apparently normal ureteric orifices is not an infallible proof that two kidneys are present, for one orifice may lead into a *cul de sac.*

iii. The observation of two healthy ureteric orifices with urine discharging from each is in very exceptional cases fallacious, for both may arise from a solitary kidney.

3. **Movements at the ureteric orifice.**—In the healthy state the orifice of the ureter will be seen to contract every few seconds, and emit a tiny jet of urine. The movement first appears at the outer end of the ridge on which the opening is placed. The ridge which lies beyond the orifice slowly swells up, and the movement spreads inward to that part of the ridge on which the opening lies. The ridge now appears to be drawn outwards, and at this moment the orifice of the ureter opens and the urine is ejected.

Variations in the rhythmic contraction of the ureter are frequently observed during a prolonged cystoscopic examination of one ureteric opening. The contractions become less and less frequent. Völcker and Joseph* have seen such pauses last three minutes, and ascribed them to over-distension of the bladder and to psychical causes. Kapsammer† has noticed intervals of eight minutes between the ureteric contractions, and he attributes them to the effect of the light and heat of the cystoscopic lamp upon the ureter. The volume of the efflux is much greater at the end of such an interval, so that the pause is due to an anomaly of ureteric contraction and not to diminished secretion.

When a kidney has been removed, the ureteric orifice of this side remains still and motionless during the cystoscopic examination. It may be inferred from this that the false duct of an undeveloped kidney will likewise be motionless, but I have not had an opportunity of examining such a case.

It does not follow, however, that a ureter which discharges no urine will shew no movement. The wave of ureteric peristalsis commences at the pelvis of the kidney, and the stimulus given by the urine as it is hurried along the duct helps to strengthen and hasten the contraction. In cases where the upper end of the duct is completely blocked and no urine or other material escapes, a feeble contraction will be observed at long intervals, as if a wave of peristalsis had been started by an occasional contraction of the over-distended renal pelvis and had spent most of its force before reaching the lower end of the duct. In a case (Mrs. S.) of hydronephrosis, recorded on page 227, no urine passed from the ureter of the diseased side, but there was a feeble gaping movement at the orifice at long intervals. Where a ureteric fistula drains away the urine from the ureter at the lower part of its course, the contraction at the vesical orifice is as powerful and the sequence as rhythmic and frequent as that of the healthy side, although not a drop of urine passes through the orifice. This was the case in a patient whose history is related on page 249, who suffered from a uretero-vaginal fistula on the left side, following a very extensive operation for uterine cancer. No difference could be observed between the appearance or movements of the two ureteric orifices in this case, although one was passing twenty ounces of urine in twenty-four hours and the other none at all. Viertel* has described such movements under the term "Leergehen."

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* *Münch. med. Woch.*, 1903.

† *Wien. klin. Rundschau*, 1904.

Where, however, the ureter has been completely severed, no contraction need be expected to appear at the vesical orifice of the duct.

4. **Pathological changes in the ureteric orifices.**—I have met with five examples of a condition which Mr. E. Hurry Fenwick has described as the "dragged out" ureteric orifice. Of the condition this observer says: "It affords the most conclusive *cystoscopic* evidence that we possess of the partial destruction of a small, often unfeelable, kidney by tuberculosis." The orifice is displaced upwards and outwards from its normal position, and lies

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* Veit's "Handbuch der Gynaekologie," B. ii., S. 171.

in the depth of a tunnel-like depression. "Instead of the ureteric orifice of the tuberculous kidney being an inch or an inch and a half from its fellow, and at the same distance from the urethral orifice, it is seen to be as much as two inches from either opening."

Of the five cases that have come under my notice there was advanced tuberculous disease of the kidney in every one.

I shall relate one case in illustration. A young man (F. C.) was sent to me by Dr. R. J. Waugh in November, 1907. He complained of abdominal pain of moderate severity which had lasted for eight months. There was occasional bilateral iliac pain, and some pain in the right loin. Two months before I saw him he had a sudden attack of hæmaturia, his urine being as dark as port wine. This continued with short intervals until I saw him. For three months there had been increased frequency of micturition, and he now made water every hour and a half, day and night. The urine was murky with pus and blood. There was no history of tuberculosis in the family. He was a well-developed lad, with red hair and a transparent complexion. The genital system was healthy. The bladder held six ounces of fluid. There were some small deposits of tubercle on the posterior wall of the bladder, and the mucous membrane was tough and fibrous looking, as if from old scarring.

The left ureter was dragged out into a tunnel and lay to the left of and behind its normal situation (Plate VI., Fig. 2). The right ureter was normal in appearance. The kidneys were not palpable or tender. A diagnosis of advanced tuberculous disease of the left kidney was made. The diagnosis rested upon the observation of the dragged-out ureter, as there were no other symptoms of disease of this kidney. The patient refused operation, but later returned to me, and on March 9th I could feel the left kidney enlarged, but a colleague who examined him could not detect it. The left ureter would only admit a catheter for two inches, and I had to abandon this side and catheterise the right ureter and drain the bladder.

Fifteen minims of indigo-carmine solution (1 – 150) were injected into the muscles of the thigh. The right urine became stained a faint green in nineteen minutes, and remained green for about an hour. The left urine was bloodstained and contained no indigo-carmine.

On March 11th I removed a large kidney which was completely destroyed by tuberculous disease (Plate VII.). The ureter was thick and hard.

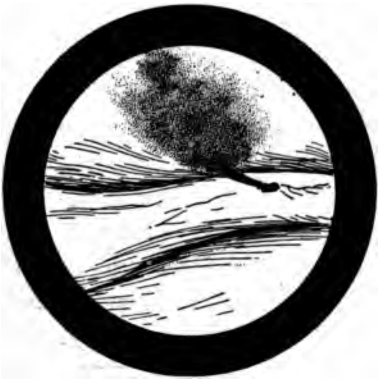

Fig. 9.—Chromocystoscopy. The left ureter is shewn at the moment when a jet of urine stained with indigo-carmine is being expelled.

CHROMOCYSTOSCOPY

A method of cystoscopic examination of the renal function has been suggested by Völcker and Joseph.* An intramuscular injection of four cubic centimetres of a four per cent. solution of indigo-carmine is made. Elimination commences in 20 minutes, reaches its height 30 minutes later, and has ceased in two hours. The authors claim that the examination of the ureteric orifices, and the observation of variations in the depth of staining of the urine issuing from each, will afford an approximate idea of the functional value of the kidneys (Fig. 9). Similar observations had previously been made in regard to methylene blue.

Variations in the type of efflux have been studied by this method. Völcker and Joseph have described a rapidly repeated or a continuous efflux with jets corresponding to waves of ureteric contraction, as occurring in compensatory

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* *Münch. med. Woch.*, 1903, S. 2028, and *Deutsche med. Woch.*, 1904, S. 536.

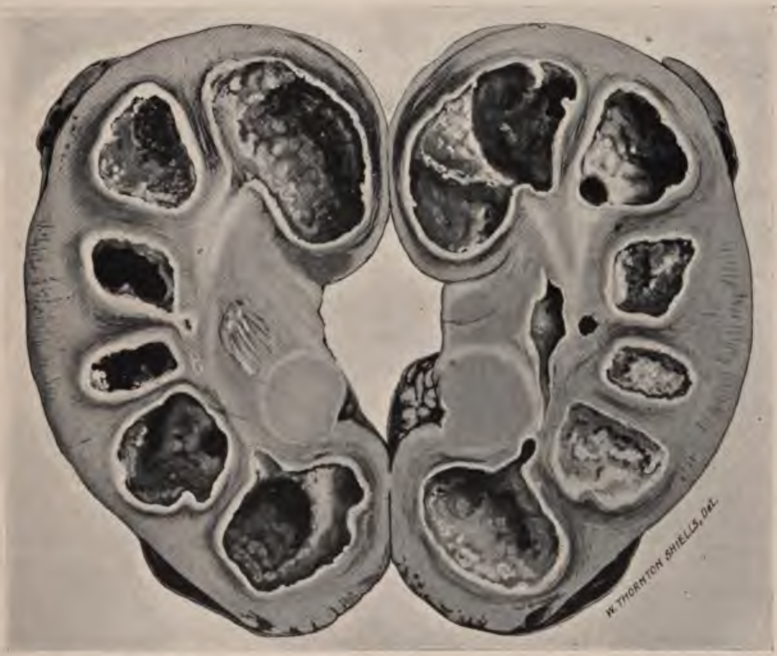

PLATE VII.—Tuberculous kidney; nephrectomy. A cystoscopic view of the "dragged-out" ureter corresponding to this kidney is shewn in Plate VI., Fig. 2.

hypertrophy; Albarran[*] noted a voluminous efflux repeated at long intervals (2 to 2½ minutes) in pyonephrosis with patent ureter, and a continuous efflux in dilated ureters.

Kapsammer[†] described a thin continuous stream in stenosis of the ureter.

This method is preferred by some (Hartmann,[‡] Legueu[§]) to the results of ureteral catheterisation. The two methods do not, however, run on parallel lines. Differences in the depth of staining of the urine of each kidney after the injection of indigo-carmine or other dyes may be observed either by examining the ureteric orifices with the cystoscope while the coloured urine is pouring from them, or by comparing two glasses which contain the separated urines collected by ureteral catheterisation. But the observation is much more accurate when the collected separate urines are examined than when the surgeon watches momentary jets of stained urine at the ureteric orifice. But in addition, the chemical and microscopical analysis of the separated urines gives invaluable information that cannot be obtained by chromocystoscopy.

At the best, chromocystoscopy is a ready clinical test of the presence or absence of a ureteral efflux. From the opacity of the jet a rough idea may be gained of the function of the kidney.

As a means of localising the position of the ureters in difficult cases and of making observations on the renal secretion where catheterisation of the ureters or separation of the urines is impossible, it may play a minor *rôle.*

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[*] *Loc. cit.*

[†] *Wien. klin. Rundschau,* 1904.

[‡] *Bull. de la Soc. de Chir.*, Paris, 1904, 421.

[§] Assoc. franç. d'urologie, Oct., 1904.

CHAPTER III

METHODS OF SEPARATION OF THE URINE OF EACH KIDNEY

Evolution of Methods—Separators—Technique of Separation of Urines—Catheterisation of Ureters—Catheter Cystoscopes—Ureteral Catheters—Sterilisation and Preservation of the Instruments

A.—HISTORICAL REVIEW

It has been the ambition of surgeons almost since the first nephrectomy to collect the urine from each kidney separately for the purpose of diagnosis.

The evolution of the instruments now in use has proceeded along certain lines, and the principles on which the different methods are based are four.

1. The occlusion of one ureter while the urine of the other is collected.
2. The removal of the urine from one ureter by suction applied to the opening.
3. The placing of a fine catheter in one or both ureters.
4. The division of the bladder into two parts, into each of which a ureter opens, and the draining of these separately.

In 1874, five years after the first nephrectomy, Dr. Tuchmann,* of the German Hospital (London), perfected an instrument by which he was able to collect the urine from one kidney. His instrument was not unlike the modern lithotrite in form, but the blades were smooth and were made to approach each other by a light spring. The application of the instrument depended upon the fact that the ureters open upon a transverse ridge. After much practice the inventor was able to pinch up this ridge with the "ureteral forceps," and thus occlude the opening. The urine which flowed into the bladder was now derived entirely from the unobstructed kidney, and was drained through openings in the shank of the instrument.

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* *Wien. med. Woch.*, 1874, 21, 22; and *Deutsche Zeitschr. f. Chir.*, v., 1875; vi., 1876.

In the following year, 1875, Lewin* succeeded in passing a fine catheter into the ureter of a female subject. By introducing his forefinger through the urethra into the bladder, he was able to locate the ureteral ridge by the sense of touch, and by this means to guide a catheter into the ureteral opening. This method, which was only applicable to the female, necessitated the use of an anæsthetic.

Grünfeld's work† on endoscopy appeared in 1881, and he described his attempts to pass instruments into the ureteral openings. For this purpose he used a straight tube with a window, and reflected light as an illuminant. He admitted that "on account of many optical and anatomical difficulties he had only succeeded in finding the ureteral openings by means of the endoscope in the female bladder."

Polk‡ suggested the introduction of a metal catheter of sigmoid contour into the bladder. The curve of the catheter was made to hug the "right pelvic wall," and the end of the curve lay across the line of the right ureter. Two fingers were introduced into the rectum and pressed against the catheter, and by this means the ureter was occluded. The lumen of the catheter meanwhile drained the urine from the other kidney. "In the female the procedure is more certain of accomplishment than in the male, because we can in a measure fix the base of the bladder by traction upon the anterior vaginal wall by means of a tenaculum hooked into it just below the cervix."

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* Volkmann's *Klin. Vorträge*, No. lxxxviii.

† "Die Endoscopie der Harnröhre u. Blase," 1881.

‡ *N. Y. Med. Jour.*, Feb., 1883.

Early in 1883 Newman, of Glasgow,[*] devised and used an electric endoscope and ureteral catheters. The electric lamp was introduced into the bladder through the speculum. Two fine elastic catheters were passed along the urethra outside the tube and manipulated into the ureters.

In 1883 Weir[†] suggested the occlusion of the ureter by the introduction of a Davy's lever into the rectum and pressing it against the ilio-pectineal line. Sands[‡] had previously tried to carry this into effect by means of the index finger. Polk[§] and Ebermann[||] endeavoured to pinch the ureter with a two-bladed instrument, one arm of which was introduced into the rectum and the other into the bladder.

Silbermann[¶] approached the ureteral opening more directly. He endeavoured by means of an indiarubber ball, which he introduced into the bladder and filled with quicksilver, to occlude one opening. The success of this method was marred by the rupture on several occasions of the rubber ball, and the outpouring of the fluid mercury into the bladder. A recent adoption of this principle is described by Rochet and Pellanda.[**] These authors have constructed an instrument carrying a rubber ball which, when distended with air, exerts a uniform pressure upon the region of the bladder base in which the ureter of the side opens while the urine is drained from the other ureter by an opening in that aspect of the instrument.

Sänger and Hegar[††] described the palpation of the lower ureter in the female from the vagina, and the former recommended the exposure and temporary ligature of one ureter through the lateral fornix. Under Sänger's direction, his assistant Warkalla* successfully performed in 1886 the temporary ligation in 10 out of 13 bodies, on which the attempt was made. Sänger concluded from these experiments as follows: "In general, ligature of the ureter from the vagina appears to be much preferable to any of the intravesical methods of occlusion of the ureter with the object of collecting the secretion of each kidney, and it is even better than direct catheterisation under the guidance of the finger in the vagina."

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[*] *Glasgow Med. Jour.*, Aug., 1883.
[†] *N. Y. Med. Record,* 1883.
[‡] *Ibid.*
[§] *Loc. cit.*
[||] *St. Petersburger med. Woch.*, 1876.
[¶] *Berl. klin. Woch.*, 1883, No. xxxiv.
[**] *Gaz. hebdom. de méd. et de chir.*, 1902, Dec. 14.
[††] *Archiv f. Gynaek.*, 1886, B. xxviii.

In 1886 Pawlik † published the description of a method he had used since 1881, by which the female ureter might be catheterised without illuminating the bladder, and without the necessity of a preparatory operation.

In one of his patients a permanent uretero-vaginal fistula had become established after a removal of the cervix by means of the thermocautery. By practising on the patient he was able to introduce a sound into the bladder opening of the ureter without the aid of a guiding sound in the ureteral fistula.

He made use of two guiding points in practising his method, the position of the trigone of the bladder and the prominence of the lower end of the ureter felt from the vagina when the bladder is over-distended. Hurry Fenwick ‡ described an instrument in the same year by means of which suction was applied to one or other ureter, and the urine collected. Catheterisation of the ureters, after opening the bladder, has been proposed by some surgeons. Thus Emmet § recommended vaginal cystotomy, Harrison perineal cystotomy, and Guyon,‖ Albarran,¶ and Iverson ** suprapubic cystotomy, as preparatory measures to ureteral catheterisation.

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* *Archiv f. Gynaek.*, 1886, B. xxix.

† *Wien. med. Presse*, Oct., 1886; and *Archiv f. klin. Chir.*, 1888, B. xxxiii.

‡ *Lancet*, 1886, Sept. 16.

§ Quoted by Müller, *Deut. med. Woch.*, 1887, No. xxxi.

‖ *Ann. d. mal. d. org. génito-urin.*, 1891, p. 744.

¶ *Idem*, and *Rev. de gynéc. et de chir. abdom.*, 1897.

** *Centralbl. f. Chir.*, 1888.

In 1887 Brenner,[*] in America, modified Leiter's posterior cystoscope by adding to it a fine tube, which opened immediately below the window. Along this a catheter could be passed and manœuvred into a ureteral opening. Tilden Brown[†] added a double channel for catheters in order to drain both ureters simultaneously. Later (1891) Nitze[‡] applied the principle to his cystoscope, placing the catheter opening upon the concavity of the beak. Modifications of these instruments have been introduced by Casper,[§] Albarran,[||] Freudenberg,[¶] and others. In 1893 Kelly[**] made use of the Sims knee-elbow position and a short, straight tube to obtain atmospheric distension of the bladder in the female. By means of reflected light he was able to examine the interior of the bladder and inspect and catheterise the ureters.

A new principle in urine separation was propounded by Lambotte,[††] of Brussels, in 1890. His idea was to create a median partition in the bladder which should divide it into two lateral halves, each of which contained a ureteral opening, and thus received the urine from the kidney. These urines could then be drained off separately. In Lambotte's instrument the septum was made of caoutchouc. The instrument and the method remained in obscurity, however, and Alfred Neumann,[‡‡] of Guben, in 1897 developed the same principle, and his instrument received wider acceptance. In 1898 Harris,[§§] of Chicago, introduced an instrument on somewhat different lines. His object was to create a median longitudinal ridge on the floor of the bladder by the pressure of a lever in the vagina or rectum, and to drain the depression on each side of this. A lever was introduced into the rectum or vagina, and this was connected with a double catheter which could be separated in the curved portion and each catheter laid apart on the base of the bladder, leaving a space between them which the pressure of the lever below the bladder base formed into a ridge. This ingenious instrument was modified by Downes * in 1900 and Nicolich † in the following year.

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[*] Deutsch. chirurg. Congress, 1887.

[†] *Annals of Surgery*, Dec., 1899.

[‡] *Ann. d. mal. d. org. génito-urin.*, Dec., 1891; "Diagnostik. Lexicon Wien.," 1894, B. iv., 191; *Centralbl. f. Chir.*, 1895, No. ix.

[§] "Handb. d. Cystoscopie," 1898; *Centralbl. f. Chir.*, 1895, No. ix.

[||] "Exploration des fonctions rénales," 1905.

[¶] Assoc. franç. d'urologie, Oct., 1904.

[**] "Operative Gynæcology," 1893.

[††] *Jour. de méd. et de chir.*, Brux., Sept., 1890.

[‡‡] *Deut. med. Woch.*, 1897, 690.

[§§] *Jour. Amer. Med. Assoc.*, 1898, p. 236.

In 1901 Dr. Luys, ‡ of Paris, described an instrument on similar lines to those of Lambotte, and this was followed in 1902 by another separator invented by Dr. F. Cathelin, § also of Paris.

B.—METHODS AT PRESENT IN USE

At the present time two methods are available for collecting the urine of each kidney separately.

In one, the bladder is artificially divided into two compartments, into each of which a ureter opens and from each of these compartments the urine is drained. This is achieved by means of "separators," of which the recently invented instruments of Luys and Cathelin represent the most perfect mechanism. These instruments will, therefore, be described.

In the second method a catheter is introduced into the ureter on one or both sides. This object is attained in two ways, either by means of the catheter cystoscope, of which the instruments of Nitze, Casper, Albarran and Freudenberg are now in use, or by a distension of the bladder with air and catheterisation of the ureters by the open method of Kelly through a tube with reflected light. The latter method is applicable only to the female bladder.

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* International Congress, Paris, 1900.

† Assoc. franç. d'urologie, 1901, p. 23.

‡ Assoc. franç. d'urologie, Paris, Oct., 1901.

§ *La presse méd.*, No. xlviii., June 14, 1902. Assoc. franç. d'urologie, Paris, Oct., 1902.

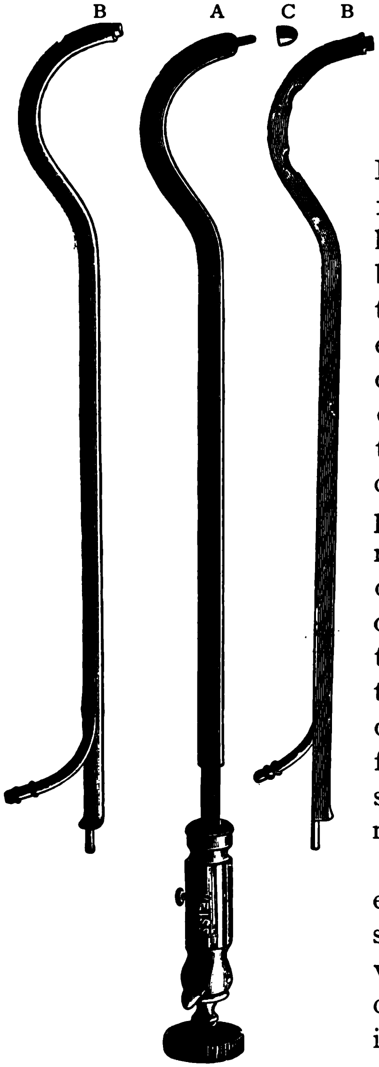

Fig. 10.—Luys' separator.

A, shank and handle; the rubber membrane has been drawn over the curve and shank, concealing the chain in the concavity of the curve; B, B, metal catheters; C, cap to unite shank with catheters.

I.—METHODS OF SEPARATING THE VESICAL URINE

The separator of Luys.—Dr. Luys' instrument (Fig. 10) consists of a shank and a handle. The shank is formed by a central metal stem, flattened from side to side, on each side of which a metal catheter is fitted. The distal end of the shank is curved to the extent of about half a circle, the curve being so placed that when the instrument is held horizontally, all of the curve except the tip of the instrument lies below the level of the straight portion of the shank. The central stem is inseparable from the handle of the instrument, but the catheters may be removed.

Attached almost to the end of the central flattened stem is a fine chain which, when loose, lies snugly in the concavity of the curve, and is connected under a bridge with a fine rod passing along the upper surface of the straight portion of the stem. When drawn tight by a screw in the handle, the chain bridges across the half-circle curve like the string of a bow. A fine rubber tube fits over the whole of the median stem, allowing a screw at the tip of the stem to pass through a small opening at its end. With the chain slack the rubber-covered central stem retains its peculiar curve; with the chain taut the half-circle curve is filled in by a rubber membrane. This forms the septum for dividing the bladder into two parts.

The metal catheters, which fit on each side of the central stem, have a flattened inner and a rounded outer surface. They fit into the handle on either side of the base of the stem, and are prolonged to its tip, being fixed to it and to each other by a metal cap which forms the point of the instrument. Openings are provided in each catheter at the upper part of the inner surface, and in the depth of the curve, and the catheter passes outwards and downwards, away from the handle, at its proximal end.

The curve of the central stem appears below the catheters, so that when lying in the bladder the lower border of the septum is formed by the stem, and not by the catheters. The handle

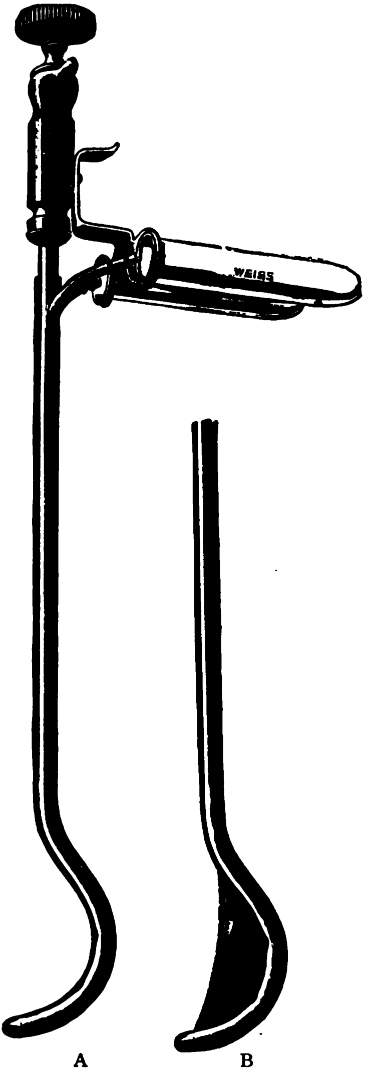

Fig. 11.—Luys' separator.

A, component parts adjusted ready for introduction; B, curve of instrument with chain drawn taut and separating membrane expanded.

is provided with a movable holder for two small glass tubes, which hang under the openings of the catheters. There is a cross-bar to ensure steadiness, and, at the end of the handle, a screw to draw the chain taut (Fig. 11).

The apparatus corresponds in size to a No. 21 French bougie. In the box containing the separator a support is provided on which the handle rests when the instrument is in place.

Technique.—The membrane having been drawn over the central stem, the catheters are fitted on either side and the tip screwed on. The instrument is then boiled for five minutes in water. Care must be taken that there is no fold or puncture in the rubber tube, for these may determine a rupture of the membrane when the chain is drawn taut.

The patient lies upon the back on an operating chair. The bladder is washed until the fluid returned into a glass vessel is clear. Six or eight ounces of fluid are allowed to remain in the bladder. Fifteen or twenty minims of a 1 to 5 per cent. solution of cocaine hydrochlorate are injected into the urethra. In the male this may be placed in the anterior urethra with a pipette and massaged back into the posterior part of the canal, or it may be introduced by means of a Guyon's syringe.

The separator is well oiled and introduced into the bladder. Dr. Luys recommends glycerine as a lubricant, and mentions a preparation by Krauss which contains gum tragacanth 2.50 grammes ; glycerine 10 grammes ; carbolic acid (3 per cent. solution) 90 grammes.

In the female subject the instrument is readily passed into the bladder. In the male the instrument passes easily until the curve lies in the prostatic urethra. It is now necessary to make this curve ride over the posterior margin of the vesical opening of the urethra and lie upon the base of the bladder. This is accomplished by depressing the handle of the instrument deeply between the thighs, and at the same time pushing gently onwards. This is the difficult part of the operation. Luys thus refers to the manœuvre : " In order to make the whole of the curved portion pass the opening into the bladder one must strongly depress the handle, meanwhile pushing gently onwards. After two or three movements of elevation and depression the instrument suddenly passes into the bladder and settles into position."

A bowl is placed in readiness between the patient's thighs to receive the fluid, which begins to flow when the beak of the instrument enters the bladder.

The patient is now gently raised into a sitting posture by raising the operating chair from the horizontal into the vertical position. The feet are supported on rests widely separated. The instrument is drawn gently towards the surgeon and held in the median line of the body with a slight upward inclination. The screw by which the chain is rendered taut is now turned, and a membranous septum formed in the bladder. A rectal or vaginal examination is made to ensure the instrument being in position.

The fluid in the bladder drains off and starts the syphonage by which the urines are drawn. The first fluid is discarded. After a short time the fluid comes away in jets of several drops rapidly following each other, and then a pause, and the tint shews that the urine has begun to flow. The tubes are now placed in position, and about 20 minutes is required to fill them with freshly secreted urine.

Luys has several times kept the separator in position for three quarters to one hour.

The introduction of this instrument is not invariably easy in the male subject. The separator passes readily until the curve lies in the prostatic urethra, and the difficulty consists in making the curve ride over the prostate. This difficulty may be increased by an abnormal rigidity of the prostatic urethra resulting from old-standing inflammation.

A weak point in the instrument is the union of the catheters and central stem by the small screw cap which forms the tip. There is a tendency for the catheter to part from the central stem, and in the female subject the short urethra allows the urine to trickle away alongside the stem.

One important objection to this instrument is that the curve is a fixed one, and the bladder base may not fit it accurately. In this the adaptable curve of the Cathelin septum has the advantage.

The separator of Cathelin.—The graduated vesical separator consists of a cylindrical tube corresponding to a No. 25 Charrière, the tunnelled beak of which is the size of a No. 2 lithotrite. (Fig. 12.) The common tube encloses three others. In the median tube runs the stem of the membrane carrier. At the vesical extremity of this is fixed a metal spring, curved on itself, which can be projected from the tube and expands in the form of a large racquet. This spring forms the frame for a rubber membrane. The membrane is projected by pushing in the shank, and retracted by withdrawing it.

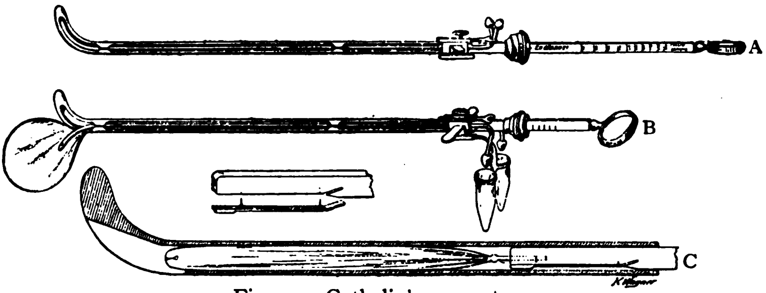

Fig. 12.—Cathelin's separator.

A, instrument with membrane retracted ready for introduction ; B, membrane projected, catheters and tubes in position during use ; C, section of vesical end of instrument.

When the instrument is in position, the membrane is held vertically in the median line in the bladder (Fig. 13). The curve of the beak allows it to lie comfortably behind the pubis, and to fit the neck of the bladder accurately.

Further, the median tube is so fashioned at its vesical extremity that the membrane, instead of unfolding in a horizontal line with the tube, expands before reaching the angle of the instrument, and thus closes the neck of the bladder and the posterior urethra.

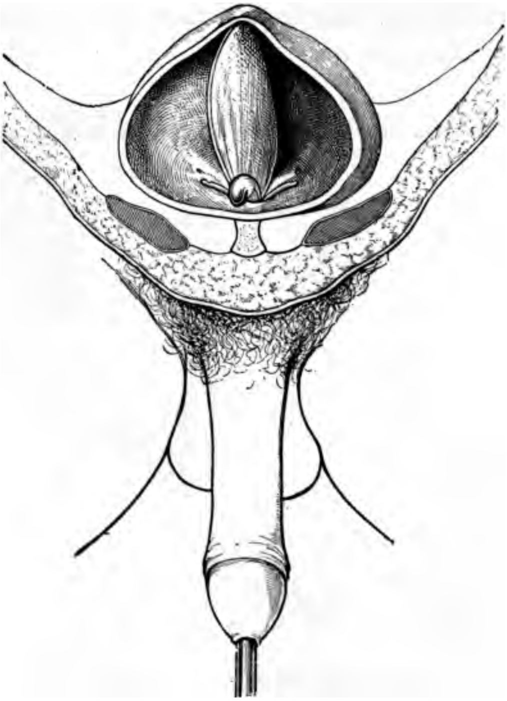

Fig. 13.—Cathelin's separator in position in bladder. Note membrane and beak in middle line and catheter on either side.

The shank, which glides in the median tube like the piston of a syringe, is graduated according to careful calculation, and the figures correspond to a vesical capacity of from 10 to 300 grammes. The two lateral tubes allow of the passage of fine catheters, which emerge from two eyes, obliquely set on the lateral aspects of the vesical end of the common tube. An important point is that these eyes are in the prostatic urethra, and not in the bladder.

A support (Fig. 14) steadies the apparatus in the median line. Graduated tubes attached to the two catheters receive the urines. Some minor changes have been made in the original instrument as experience has dictated. The catheters are now made of metal, and a cross-piece has been added to the handle.

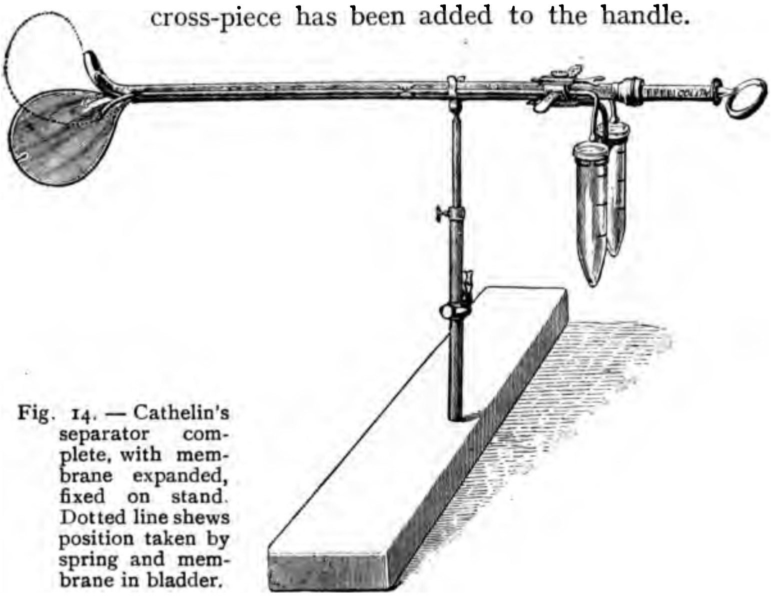

Fig. 14. — Cathelin's separator complete, with membrane expanded, fixed on stand. Dotted line shews position taken by spring and membrane in bladder.

Technique.—The tube and membrane are sterilised in boiling water. The patient lies on the back with flexed knees. The bladder is washed out until the fluid returns clear, and at the same time the exact capacity of the viscus is measured. The bladder is filled with fluid until the patient feels the desire to micturate. The instrument, well oiled, is introduced, and when it lies in the bladder the two catheters are passed forward for 3 or 4 centimetres, according to the capacity of the bladder. The instrument is gently drawn towards the surgeon until the resistance of the pubis is felt against the beak.

The instrument is held in an almost horizontal position, inclined very slightly upwards. The shank is now pushed on, the markings on it being watched, until the figure corresponding to the previously estimated bladder capacity is reached. The expanded membrane now fits the bladder cavity and the fluid is allowed to flow off. The instrument is supported on a stand, and the two tubes are placed in position to receive the separated urines. The patient remains lying upon the back during the operation (Fig. 15).

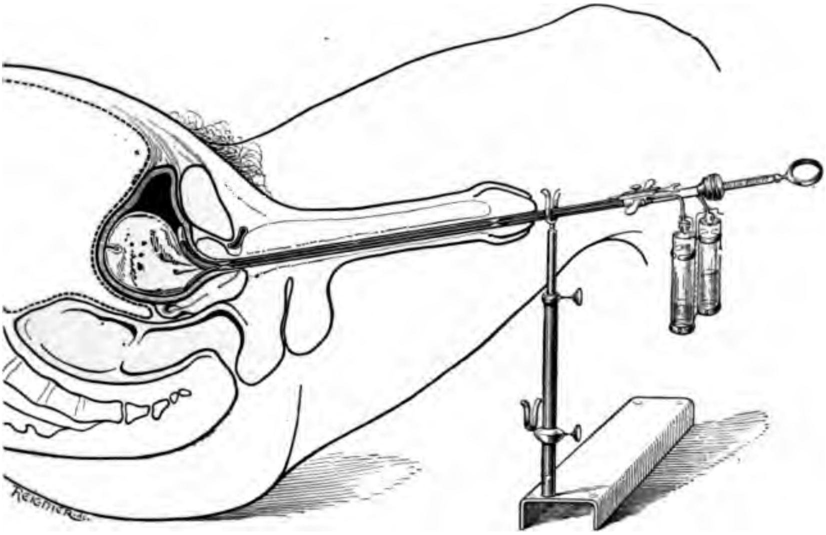

Fig. 15.—Cathelin's separator in position in male subject.

The curve of the beak of this separator renders its introduction easy, but the large calibre of the instrument is a disadvantage. In the male subject, the curve of the septum is adaptable to the contour of the bladder base, which gives it an advantage over the Luys separator.

Instruments have been constructed by Lluria* and Boddaert† on lines similar to those of Cathelin's instrument.

* Congrès de Madrid, 1903.

† Quoted by Albarran, "Exploration des fonctions rénales," 1905.

The calibre of these more recent separators is reduced, and the membrane is projected in such a manner that it fits the floor of the bladder with greater precision.

2.—CATHETERISATION OF THE URETERS

The catheter cystoscope.—There are several varieties of catheter cystoscope at present in use. I shall shortly describe those of Nitze, Casper, Albarran, and Freudenberg.

The principle underlying each of these instruments is the same. Along the upper or under surface of the ordinary cystoscope runs a tunnel which opens just short of the prism window. When the ureteral catheter is passed along this tunnel and projected from the opening, the point is seen on looking through the prism, and may be guided into the ureteral opening.

The point of the catheter projects from the tunnel at an angle with the shaft of the cystoscope, but not so nearly perpendicular to it as to allow the tip of the catheter to touch the bladder wall before it passes out of the field of vision. Some contrivance is therefore required to tilt the point of the catheter away from the line of the shaft. This is accomplished by two different mechanisms, one of which was introduced by Albarran and the other by Casper. Albarran's mechanism consists in a tiny movable gutter lying on the floor of the internal opening of the tunnel, which can be raised to a vertical position by means of a screw at the optical end of the instrument. In Casper's cystoscope the internal end of the floor of the tunnel rises suddenly to the opening, and the sliding roof of the tunnel (*see* description of the Casper instrument) when pushed in against the projecting point of the catheter so presses it against the other lip of the opening that it is made to stand up vertically from the shank of the instrument. The outflow of urine or lotion alongside the catheter in the tunnel is prevented by a leather washer at the proximal end. The tunnel may be provided with a septum and two separate inlets, so that two catheters are used simultaneously.

Nitze's catheter cystoscope.—The most recent model of this instrument consists in an ordinary Nitze cystoscope (Fig. 16) on the upper or concave surface of which is a single or double tunnel for catheters. The beak is small, and has a gentle curve which greatly facilitates its passage through the urethra.*

The Albarran movable gutter for controlling the direction of the catheter is used. The tunnel is fixed in its whole length except at the last quarter of an inch, which carries the internal opening and the Albarran gutter. This part is attached to a flat strip of metal which is movable by a screw at the proximal end of the instrument, and which forms the floor of the tunnel. This is fixed in position by a special screw and may be removed to allow of its being cleaned.

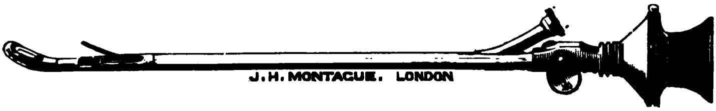

Fig. 16.—Nitze catheter cystoscope.

The current is admitted by means of a double grip contact, which carries the switch and allows the instrument to rotate while it is held stationary.

The eyepiece is flat, and when not in use is covered by a metal cap.

The flat eyepiece allows the eye to stray from the field, and a bell-shaped metal eyepiece may be added. I am accustomed to use a Nitze instrument so modified, and have found it meet my requirements.

To this instrument may be attached an apparatus

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* This beak was, I believe, originally used by Hurry Fenwick as a modification of Leiter's cystoscope. It is also in use in the Albarran instrument.

(Fig. 17) introduced by Mr. R. J. Willan,* for the purpose of protecting the ureteral catheter during introduction. The apparatus is attached to the ocular end of the catheter tunnel by means of a metal screw. This screw supports two rods (A) to which a cone is attached. On the cone is fitted a piece of rubber tubing 22 inches long with one-eighth inch bore. The ureteric catheter lies in the rubber tube and passes from it across the open space between the metal rods (B) into the catheter tunnel, this being the only part at which it is exposed. The catheter is manipulated by sliding the finger and thumb up and down along the metal rods.

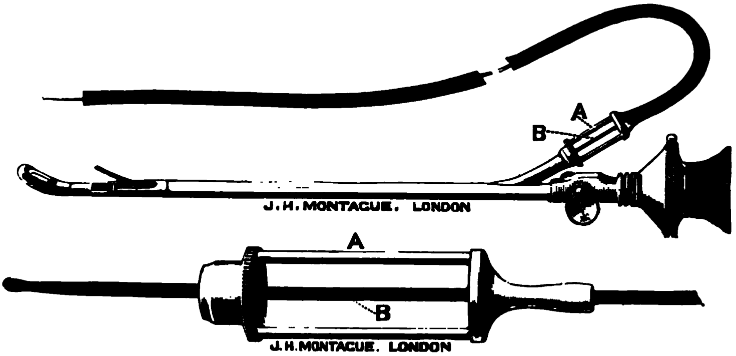

Fig. 17.—Aseptic ureteric catheter sheath attached to modified Nitze catheter cystoscope.

Casper's catheter cystoscope.—Along the upper surface of the instrument runs a gutter which terminates just short of the window by rising rapidly to its level. Along this gutter is passed a fine single or double tube, the floor of which is wanting for about an inch at the distal end. This carries the ureteral catheters, which are bent away from the shank at the distal end of the gutter by the upward inclination of the floor.

A cross-bar, fixed to the right-hand side of the base of the instrument, falls down into a vertical slot attached to the catheter tube. This cross-bar may be pushed towards the beak or pulled towards the ocular end of the cystoscope, and in so doing pushes the projecting point of the catheter against the inclined termination of the gutter and raises the tip, or releases it and lets the point drop (Fig. 18). The beak of the instrument is long, its attachment to the shaft angular, and the shoulder, where the catheter tunnel commences behind the window, is abrupt. These defects hamper the introduction of the instrument through the male urethra.

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* *Lancet*, May 4, 1907.

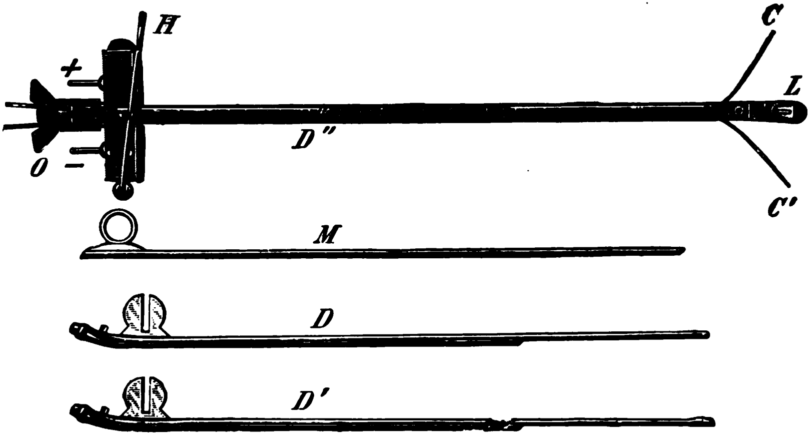

Fig. 18.—Casper catheter cystoscope.

D D′, tubes which carry ureteric catheters and form roof D″ of gutter on upper surface of shaft; H, lever which fits into slot in roof and pushes it inwards or outwards, raising or lowering points of catheters; M, roof forming single channel; L, lamp; O, ocular end of cystoscope.

The electric current is introduced by means of a small plate and pins which rotate with the instrument.

Albarran's catheter cystoscope.—In this instrument the catheter portion is separable from the optical, which may be used separately as an ordinary cystoscope (Fig. 19). The telescope has a small calibre, and immediately proximal to the window is a notch into which fits the movable gutter of the catheter portion. At the distal end of the tunnel thus formed is Albarran's small movable gutter for raising the point of the catheter (Fig. 19 B).

In the sheath are two tunnels, one for the catheter and the second for the addition or withdrawal of fluid from the bladder. The beak has a gentle curve. The current is introduced by a contact piece similar to that used in the Nitze instrument. The whole instrument has a calibre equal to No. 23 Charrière.

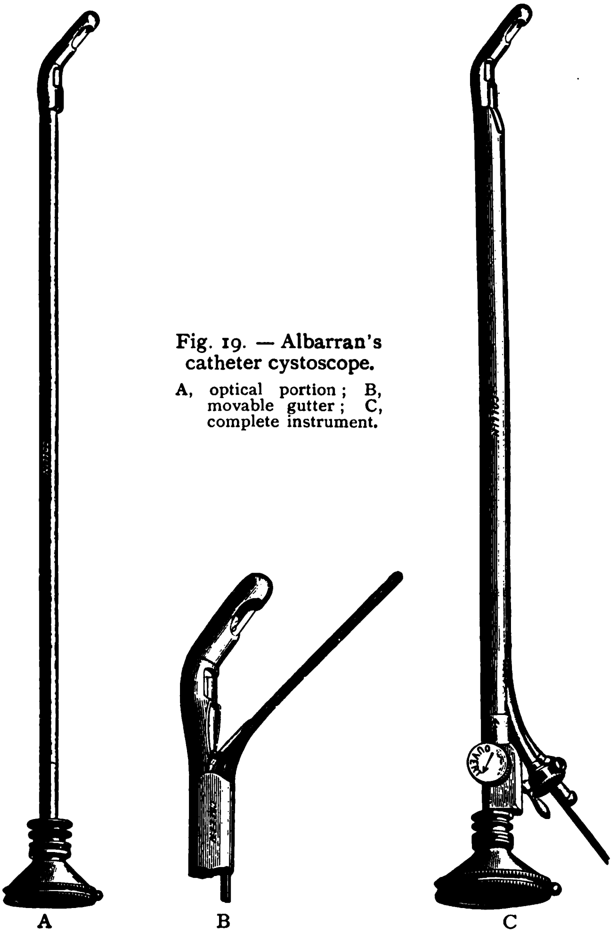

Fig. 19. — Albarran's catheter cystoscope.

A, optical portion; B, movable gutter; C, complete instrument.

The cystoscope of Freudenberg.*—In this instrument

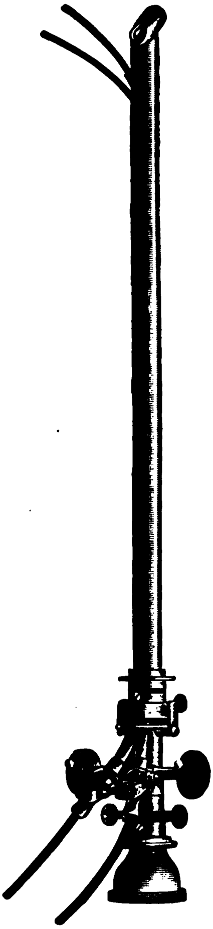

Fig. 20. — Freudenberg's catheter cystoscope complete.

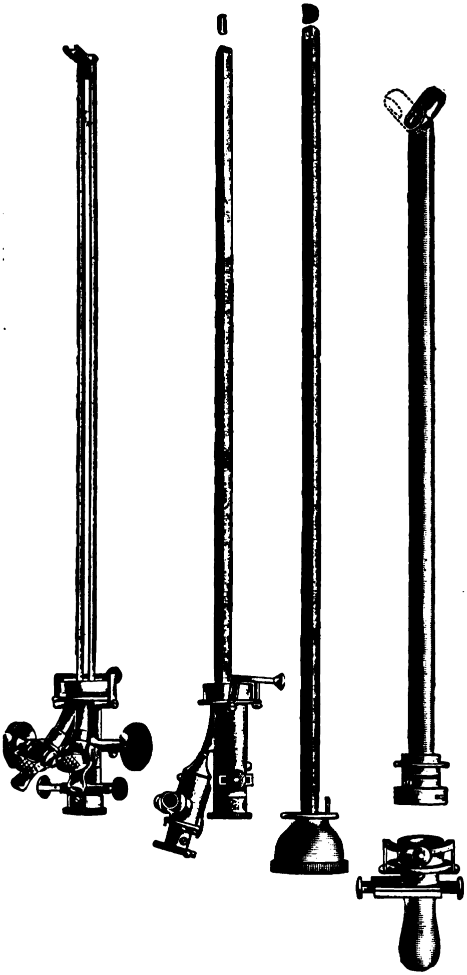

Fig. 21.—Parts of Freudenberg's catheter cystoscope.

(Fig. 20) there are two points of difference from those already described. The lamp, prism, and opening for the ureteral catheters are placed on the side corresponding to the convexity of the beak, so that the latter does not interfere with the approach of the instrument to the ureteral opening during the catheterisation. Further, it is unnecessary to turn this instrument round when about to withdraw it from the bladder, and the inconvenience of crossing or dragging upon the catheters is thus avoided.

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* VII. Congrès Assoc. française d'Urologie, Paris, Oct., 1904 ; *Centralbl. f. Chir.*, 1904, No. li. ; *Monatschr. f. Harnkrankh. u. Sexuel Hygiene*, 1906, H. 2.

The second peculiarity consists in a plate being placed between the catheter and the telescope (Fig. 21). The telescope and this movable floor can be removed, leaving a hollow metal tube in which the catheters lie free. This tube is easily withdrawn, leaving the catheters in place. The instrument may be used as an irrigation cystoscope by withdrawing the optical apparatus. Ureteral catheters with an oval lumen may be used with this instrument.

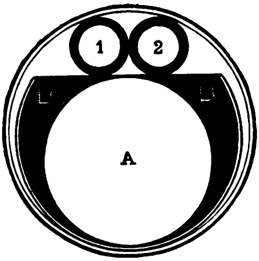

Fig. 22.—Transverse section of Freudenberg's catheter cystoscope.

A transverse section is seen in Fig. 22, which shews the telescope A and B B, above which are the catheter carriers 1 and 2.

Ureteral catheters.—The catheters used for introduction into the ureter are about 30 inches long and correspond to a No. 5, 6, 7, or 8 Charrière. Several sizes are necessary, for the openings of the ureters vary in calibre in different individuals. A brass wire stilette prevents bending and coiling; it is removed before the catheter is used. The end of the catheter may taper to a point with a fine olivary bulb, or it may be rounded. There are one or two eyes placed laterally. The outlet of the catheter may be trumpet shaped, but if the cystoscope is to be withdrawn this trumpet end must be cut off (Fig. 23). Albarran's catheters, made by Gaillard, of Paris, are finely finished instruments. In one form the perforated extremity is cut "*en bec de flûte*," and there are besides two lateral openings. There is also a slight thickening immediately proximal to the second eye, which prevents any urine passing down alongside the catheter.

These catheters are graduated in centimetres in different colours along their whole length, and at each 10 centimetres there is a mark recognisable through the cystoscope.

Professor Nitze* introduced in 1902 a ureteral catheter specially constructed to prevent the escape of urine alongside the instrument. The catheter has a double lumen and from each lumen an eye opens near the end of the instrument. Surrounding the catheter near its inner end, but proximal to the first eye, is a small balloon of fine rubber, and into this opens the eye of the second lumen. A stopcock with a lateral and terminal ways allows entrance to the lumen which opens into the balloon or that which opens beyond it. The "occlusion catheter" (*Okklusivkatheter*) is passed into the ureter, and about 30 minims of fluid injected into the balloon, so that it swells up and occludes the ureter below the eye of the catheter, thus preventing any escape of urine alongside the instrument. A few drops of methylene blue solution are injected into the ureter and colour the urine from this ureter, and the absence of colouration in the urine drained from the bladder shews that there is no escape of urine alongside the ureteric catheter. For the use of this catheter a large

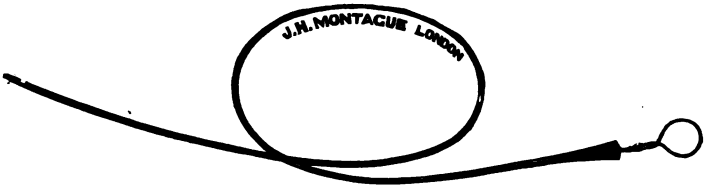

Fig. 23.—Ureteral catheter.

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* Congrès de Madrid, 1902; *Centralbl. f. d. Krankh. d. Harn. u. Sex. Org.*, 1905, B. xvi., H. 3.

bore cystoscope tube is necessary, and the whole instrument corresponds in size to No. 25 Charrière. Further, Nitze admits that in 10 per cent. of cases the vesical orifice of the ureter is too small to admit the "occlusion catheter," and must be dilated to the size of a No. 8 or 9 Charrière. This is a grave disadvantage.

Mr. J. H. Montague has made for me a ureteral catheter which differs in some particulars from those just described (Fig. 24). The catheter is 30 inches long, and is marked in alternate black and yellow divisions of half an inch each. One white band surrounds the catheter at 6 inches, two at 12 inches, three at 18 inches, and so on, one band being added for every 6 inches. The outlet is cut obliquely for the convenient introduction of a syringe point.

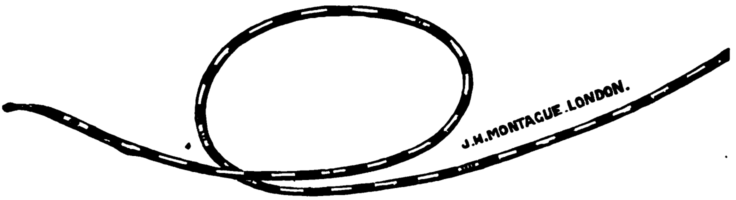

Fig. 24.—Author's ureteric catheter.

The point of the catheter is shaped as if the tube were cut obliquely, and the longer lip is tailed off to form a fine end, which is flattened and gradually becomes gutter-like as it approaches the opening of the lumen. The tip of this tongue is rounded and bulbous, and bends slightly, so that the gutter commences in the concavity. This curve somewhat facilitates the introduction of the instrument into the opening of the ureter, and also helps to keep the mucous membrane of the ureter from closing upon the opening of the catheter. This opening is as nearly terminal as is compatible with the retention of a fair degree of strength in the tip of the instrument. Behind this opening are two others, on different aspects and at different distances from the end. I have adopted Albarran's method of preventing urine passing the openings and escaping alongside the instrument—namely, a thickening of the catheter immediately proximal to the last eye, but this thickening, instead of being ring-like, surrounds the instrument in an annular manner.

The circumference of the catheter corresponds to a No. 6 Charrière, and of the bulbous thickening to a No. 7 Charrière.

STERILISATION AND PRESERVATION OF THE INSTRUMENTS

The cystoscope with the tunnel for carrying the ureteral catheter and the mechanism for its manipulation requires careful cleaning and sterilisation.

In some of the instruments this is more easily carried out than in others.

When the catheter conductor is in the form of a tube the interior of this should be carefully cleaned before and after each use of the instrument.

The instruments may be made aseptic by boiling, by exposure to formalin vapour, or by washing with antiseptics.

The cystoscopes that consist wholly of metal may be boiled, but the reflecting layer of the prism loses in sensitiveness from the heat. Further, when the instrument cools there is a condensation of moisture in the interior of the telescope, and this renders the optical apparatus useless, or interferes with the distinctness of the picture.

Albarran has had a formalin steriliser made by Collin, of Paris, in which a spirit lamp vaporises formalin and raises the temperature to 60° C. The cystoscope is allowed to remain in this atmosphere for half an hour.

Kollmann and Wossidlo* have introduced a formalin steriliser in which the ocular end of the cystoscope is made for me a wide glass tube (1 inch in diameter) which is open at both ends (Fig. 27). One end is fitted with a hollow rubber cork which carries a perforated box containing tri-oxy-methylene, a granular formalin compound, while the other end is closed with a rubber cork pierced by the special syringe just described. The object of using an open tube instead of one closed at one end is that moisture rapidly collects in the closed tube, and it is difficult to keep it clean. The tube should be left open at both ends for an hour or two now and again.

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* *Centralbl. f. d. Krankh. d. Harn. u. Sex. Org.*, 1901.

Unless these precautions are carefully observed the ureteral catheters rapidly deteriorate, their surface becomes rough, and a risk of infection is incurred.

CHAPTER IV

THE OPERATION OF CATHETERISATION OF THE URETERS

Preparation of the Bladder—Finding and Approaching the Ureteric Orifice—Introduction of Catheter—Direct Catheterisation of the Ureters by Kelly's Method—Fallacies, Difficulties, and Dangers of Catheterisation of the Ureters—Choice of an Instrument for Separation of the Urines

FOR the catheterisation of the ureters certain conditions are requisite: a clear medium, sufficient distension of the bladder, and an anæsthetic urethra.

The patient lies upon his back on a couch or operating table with the pelvis raised on a hard cushion. The surgeon stands on the right side. If an examination chair is available the patient reclines upon this, with the knees flexed and the feet supported on rests, and the surgeon faces the perineum.

No general anæsthetic is required. Ten minutes before commencing the examination 20 minims of a 2 per cent. solution of cocaine are instilled into the prostatic urethra with a Guyon's syringe, or introduced into the anterior urethra with a pipette, and massaged back through the membranous urethra. The bladder, apart from its trigone, possesses slight sensibility under normal conditions, and the instrument should not touch its walls. A hypersensitive bladder base may be treated by the addition of a few drops of cocaine solution to the wash, or 30 grains of antipyrin may be used in the same way about half an hour before the examination. Albarran recommends the following formula: antipyrin 2 grammes, tincture of

opium 15 minims, water 100 grammes. In exceptional cases. where vesical spasm is present, a general anæsthetic is desirable.

Where the bladder is healthy no preliminary washing is required. A gum-elastic catheter lubricated with glycerine is passed, and the bladder is slowly filled with warm boracic lotion by means of a hand syringe* until twelve ounces have been introduced (Fig. 28).

Where cystitis is present careful and painstaking washing is necessary. The wash is examined in a glass vessel from time to time to note progress, and the surgeon should not rest satisfied until a clear medium is obtained. It is sometimes necessary to submit the patient to a course of washing extending over several days, so that the examination may be made under the best possible conditions.

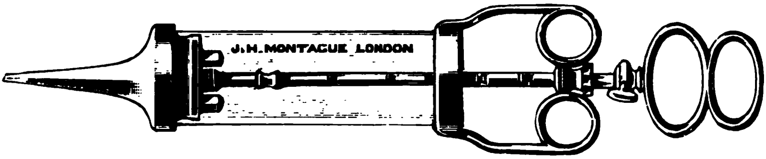

Fig. 28.—Glass syringe for bladder washing.

Bleeding during the washing is best treated by using a very weak solution of silver nitrate (1 in 10,000 or 15,000). The silver solution is followed by further irrigation with boracic solution. Solutions of extract of suprarenal gland (one drachm to the pint or stronger) may be used, but give disappointing results. A distension of twelve ounces should be aimed at, for with this the ureters are readily approached. In the female bladder

a good distension is especially necessary, and the pelvis should be well tilted, for the bladder base, from its relation to the vagina, lies on the same plane as the floor of the urethra, and it may be difficult to raise the beak of the instrument away from the floor of the viscus so as to manœuvre the catheter into the opening of the ureter.

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* A funnel and rubber tubing is often used for bladder washing, and occasionally a reservoir at a height provides the supply and distends the bladder by hydrostatic pressure. With these methods it is not easy to make certain of the exact quantity of fluid that has been introduced, and the latter is dangerous from the high pressure that is developed. Neither method should be employed when the patient is unconscious. A syringe must be used with gentleness; it transmits to the practised hand a sufficient indication of the intravesical tension. The syringe should have a known capacity.

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When the ureteric opening comes into view the cystoscope will lie with its long axis in the middle line of the body and the beak twisted towards the side of the observed ureter. By carrying the ocular end of the instrument towards the opposite thigh the window and catheter

opium 15 minims, water 100 grammes. In exceptional cases. where vesical spasm is present, a general anæsthetic is desirable.

Where the bladder is healthy no preliminary washing is required. A gum-elastic catheter lubricated with glycerine is passed, and the bladder is slowly filled with warm boracic lotion by means of a hand syringe* until twelve ounces have been introduced (Fig. 28).

Where cystitis is present careful and painstaking washing is necessary. The wash is examined in a glass vessel from time to time to note progress, and the surgeon should not rest satisfied until a clear medium is obtained. It is sometimes necessary to submit the patient to a course of washing extending over several days, so that the examination may be made under the best possible conditions.

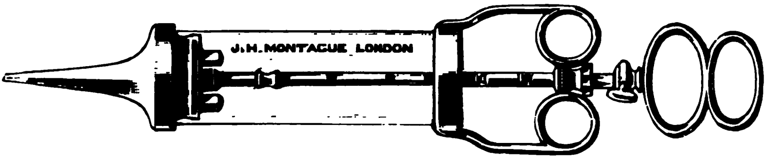

Fig. 28.—Glass syringe for bladder washing.

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opening will be found to approach the ureteric opening. The window now lies above and slightly to the inner side of the opening. The catheter is pushed on so that the point lies about the middle of the field of vision (Fig. 29). A touch of the elevating screw may make the tip of the catheter sink into the opening or approach the bladder wall so close to it that a very slight movement of the cystoscope will push it over the edge into the orifice. But the point may still be a little distance above the surface, and the ocular end of the instrument must be slightly raised so that the beak drops towards the bladder base. It is a bad plan to depend too much upon the elevating screw or to project too great a length of catheter when the orifice is still at a distance. Most of the manœuvring should be done with the cystoscope as a whole and the elevation and pushing on of the catheter left for the final stage when the window is close to the opening. If the elevator be raised too much it will bend the catheter so acutely as almost to kink it. The freedom of movement of the catheter is thus restricted, and its surface is scraped and abraded by the edge of the opening of the tunnel.

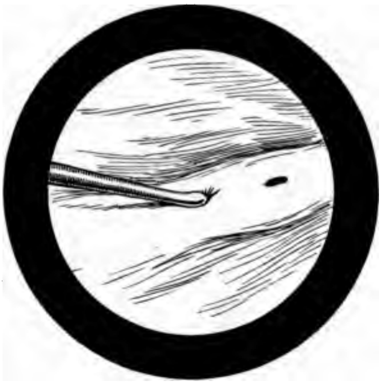

Fig. 29.—Catheter approaching ureteric orifice.

The orifice should be approached from above and from the median side. The catheter sinks between the lips of the opening and is slowly and gently pushed onwards by the disengaged thumb and forefinger of the right hand, the left hand meanwhile steadying the ocular end of the instrument and holding it firmly in position (Fig. 30). As the catheter enters the ureter and passes along the submucous part of the ureter the outer end of the ureteric ridge beyond the orifice of the duct is raised up for one-eighth of an inch or more. The elevator may now be lowered and the catheter glides more easily. The distance to which it is pushed along the ureter will vary with the purpose for which it is introduced. If it is intended only to drain the urine it will be sufficient to introduce from 4 to 6 inches of the catheter into the ureter. This is the minimum, for a shorter length of catheter may slip out of the duct during the further manipulation.

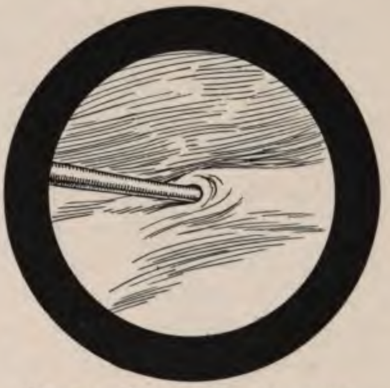
Fig. 30.—Catheter lying in ureter.

If it is intended to catheterise both ureters and a double channel cystoscope is being used, the beak is now turned towards the second ureter and the ocular end of the cystoscope moved towards the opposite thigh. The same manœuvring is carried out on the second side that has been detailed in describing the passage of the catheter into the first ureter. When the second catheter is in place the elevator is lowered, the light switched off, and after pushing some slack catheter into the bladder the cystoscope is gently withdrawn. In order to do this the beak must be turned upwards and a strain will be put upon the catheter if sufficient slack has not been pushed into the bladder. The Freudenberg instrument is specially designed to facilitate the withdrawal of the cystoscope. In it the ocular apparatus may be removed, leaving a hollow tube in which the catheters lie loosely, and which is readily slipped out without dragging upon them. I use a single barrel catheter cystoscope, and after catheterising one ureter I withdraw the cystoscope, reload it with a second catheter, and reintroduce it if the second ureter is to be catheterised. This has the disadvantage of a double introduction of the cystoscope along the urethra and the second time alongside the first ureteral catheter, but the instrument is less bulky.

Each catheter is fixed with a piece of adhesive plaster to the inner surface of the thigh of the side to which it belongs. If this is not done they are easily crossed in the urethra and it is impossible to tell to which kidney either catheter belongs. A bottle labelled " right " and another " left " is placed between the thighs to receive the ends of the catheters. The first fluid is discarded, for some of it is derived from the fluid filling the bladder. A fine catheter should be passed into the bladder, and this viscus emptied of fluid and the catheter withdrawn. The cushion is removed from beneath the pelvis and the patient placed in a comfortable position.

It is not always necessary to catheterise both ureters. When the bladder is healthy a catheter may be passed into one ureter and the cystoscope withdrawn. A urethral catheter is now passed into the bladder and left in position. This drains the second ureter through the bladder. This method is open to the objection that the urine is not obtained directly from the ureter but across the bladder, and might be contaminated in the passage. It must be ascertained, therefore, by cystoscopic examination that the bladder is healthy. Further, some urine from the catheterised ureter may pass alongside the catheter and escape into the bladder and be collected as the secretion of the second kidney. This is prevented by the means already noted in describing ureteric catheters.

The urine which passes from the catheters flows in a continuous stream when the eye is in the bladder, but when it lies in the ureter it drips away intermittently. There are four to six drops in rapid succession, then a pause of about six seconds, and then another succession of drops. If the catheter be pushed on into the pelvis of the kidney, this characteristic rhythm disappears, and the drops fall continuously. Some patients complain of colicky abdominal pain during the time that the ureteric catheter is in position, and a few have suffered from vesical spasm. A hot fomentation applied to the abdomen will relieve these symptoms. It is very rarely necessary to remove the catheter.

When the ureteral drainage is completed the catheters are gently withdrawn.

Direct catheterisation of the ureters (Kelly's method).—

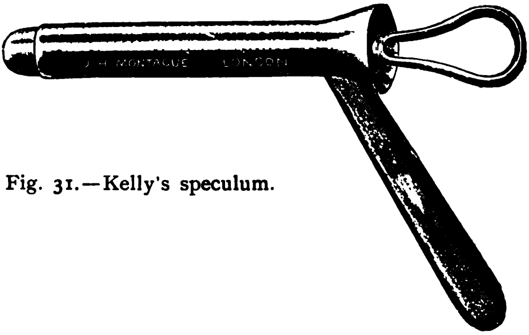

Fig. 31.—Kelly's speculum.

In 1893 Howard Kelly, of Baltimore,* introduced a method of examination of the female bladder which he uses also for catheterisation of the ureters. The method has three essential features :—

1. Atmospheric dilatation of the bladder induced by posture.
2. The introduction of a straight speculum.
3. The examination of the mucous surface of the bladder by reflected light or an electric headlight.

Pawlik† has since modified this method by dilatation of the urethra under anæsthesia so as to admit a large speculum, and the examination by means of a small electric light introduced into the bladder through the speculum.

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* *Johns Hopkins Bull.*, Nov., 1893; *Amer. Jour. of Obst.*, Jan., 1894.

† *Centralbl. f. Gynaek.*, May 5, 1894.

Kelly's specula (Fig. 31) are plated metal cylinders 3½ inches long and equal in diameter throughout. There is a funnel-shaped expansion at the outer end of the speculum, and a handle 3 inches long is attached to the funnel. The specula are made in various numbers from 5 to 20, each number representing the diameter of the cylinder in millimetres. Each instrument has an obturator, which is used during introduction.

A dilator (Fig. 32) is used to enlarge the orifice of the urethra to the proper size. It is graduated from point to base in millimetre diameters. An evacuator is used to empty the bladder of any remaining drops of urine that cannot be removed by catheter, and also to remove the urine which accumulates in the bladder during a prolonged examination. It consists of a rubber exhausting bulb and fourteen inches of fine rubber tubing, and at the bladder end a small hollow perforated metal ball.

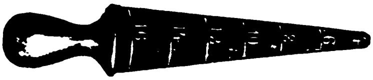

Fig. 32.—Kelly's dilator.

Technique of the examination.—The lower bowel is emptied, and immediately before the examination the bladder is emptied in a sitting or standing position. General anæsthesia is only necessary in nervous women. Local anæsthesia is obtained by introducing a pledget of cotton wool soaked in 10 per cent. cocaine into the urethra for five minutes before the examination. Two positions may be used—(1) the elevated dorsal, and (2) the knee chest.

" The dorsal position is the more convenient to use, and the least trying to the patient, but it is only of service in thin patients, and the atmospheric expansion is not so good ; the bladder of a fat woman will rarely distend at all in this position." The buttocks are raised 8 or 12 inches above the table level. The speculum is introduced, the obturator withdrawn, and the atmospheric pressure distends the bladder.

If the bladder does not expand, Kelly recommends that the patient be placed for a minute in the knee-elbow position, and air let in with a catheter. The patient is then placed on her back, with hips elevated, taking care to keep the pelvis all the time well above the level of the abdomen.

"The knee-chest position is the one position most satisfactory and applicable in all cases." The patient kneels with the knees slightly separated close to the end of the table and lets the back curve in with the buttocks well raised. The side of the face lies on the table. The patient may be held by assistants in this position, if an anæsthetic is required, or an apparatus (Dr. G. B. Millar's) may be used to sling her.

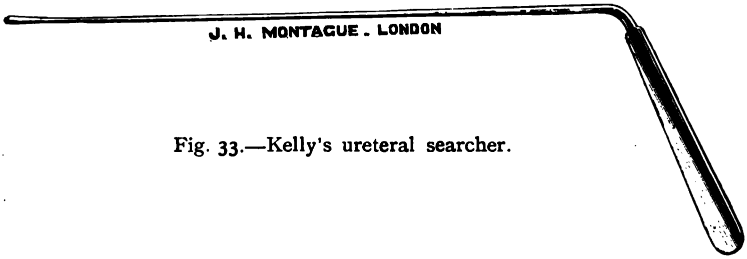

Fig. 33.—Kelly's ureteral searcher.

The speculum is introduced and light projected through it from a forehead mirror reflecting from an electric lamp held over the sacrum. The ureteral openings are located and are examined with a ureteral searcher (Fig. 33). Catheters may be passed through the speculum into the ducts. Kelly uses metal catheters if the urine merely requires to be drawn, but flexible catheters with a stylet are required if it be intended to introduce the instrument far into the ureter.

After an examination the bladder is emptied by introducing a catheter and gently lowering the patient to the horizontal.

made for me a wide glass tube (1 inch in diameter) which is open at both ends (Fig. 27). One end is fitted with a hollow rubber cork which carries a perforated box containing tri-oxy-methylene, a granular formalin compound, while the other end is closed with a rubber cork pierced by the special syringe just described. The object of using an open tube instead of one closed at one end is that moisture rapidly collects in the closed tube, and it is difficult to keep it clean. The tube should be left open at both ends for an hour or two now and again.

Unless these precautions are carefully observed the ureteral catheters rapidly deteriorate, their surface becomes rough, and a risk of infection is incurred.

a good distension is especially necessary, and the pelvis should be well tilted, for the bladder base, from its relation to the vagina, lies on the same plane as the floor of the urethra, and it may be difficult to raise the beak of the instrument away from the floor of the viscus so as to manœuvre the catheter into the opening of the ureter.

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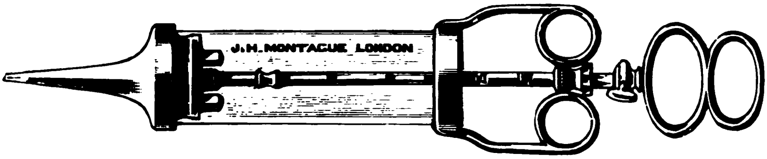

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Fallacies, difficulties and dangers of catheterisation of the ureters.—In endeavouring to draw urine from one kidney by means of a ureteric catheter, there are some fallacies that must be borne in mind.

For some minutes after the passage of the instrument no urine may flow from the catheter. A temporary cessation of function appears to occur in some cases. This is seldom prolonged. In my own cases it has only been observed where no fluid had been drunk for some time before the examination.

I now invariably give a diuretic (hot tea or Contrexéville water or theosin) half an hour before commencing the examination, and if no urine appears from the catheter I conclude that this is due to some other cause.

The catheter may become blocked with clot, thick pus, or even with gravel. When the kidney is known to be bleeding, or where semi-solid pus has been observed coming from the ureter, the cause of the blockage is apparent. A drachm of boracic solution may be cautiously injected into the catheter by means of the small syringe already described, and this may free the lumen. If the efflux from the ureter is almost solid pus, no urine need be expected to flow from the catheter.

It may happen that the eye of the catheter becomes blocked by the mucous membrane of the ureter falling upon it. If the catheter be advanced or withdrawn a little the opening will be freed, and once the flow is established no further trouble will be experienced.

Blood may appear in the urine when the catheter is introduced. This is due to an abrasion of the mucous membrane of the ureter. The bleeding is slight. If the urine flows clear at first and becomes gradually tinged with blood after the catheter has been in place for some time, the blood probably comes from a mucous membrane which is congested by the presence of the catheter.

Urine sometimes escapes alongside the catheter into the bladder. The quantity is not, however, sufficient to vitiate the result. This may be avoided by choosing a catheter of sufficient size to fit the ureter and by using one which has a thickened segment proximal to the eye.

The difficulties which attend the catheterisation of the ureters are, firstly, those of cystoscopy. The surgeon who would perform the operation and obtain reliable information must be a skilled cystoscopist, and this at once narrows the application of the method. This has been raised as an objection against the method, but it is none. It is open to many to acquire the necessary skill, and it is to the advantage of those suffering from renal diseases that they should do so.

Apart from this, however, there are other difficulties.

An enlarged prostate may render the use of the ureteral catheter impracticable. This does not apply to all cases of enlargement of the prostate, for a slightly enlarged organ, or one in which a small nodule projects into the bladder, need not interfere with the operation. But the number of cases of enlargement of the prostate in which information concerning the function of one kidney is desired is very small. The problem in these cases is the estimation of the total renal function.

A tuberculous prostate may interfere with the introduction of the cystoscope from the distortion of the urethra that it frequently produces. In these cases the free movement of the instrument in the bladder may also be retarded, and the prostate and bladder are intolerant of instrumental interference, so that a rise of temperature and vesical distress is likely to follow the operation. I therefore look upon prostatic tubercle as a contra-indication to separation of the urines, unless the necessity for accurate information upon the subject is imperative.

A stricture must be effectually treated before any method of urine separation can be adopted.

The presence of cystitis raises the problem of infection of the catheterised ureter, which I shall discuss later. In acute cystitis it is usually possible to catheterise the ureters under a general anæsthetic. The bladder may be so irritable that even a small quantity of injected fluid is promptly discharged, and sometimes the catheter is shot from the urethra by the spasm. It is seldom, however, that with care and patience the bladder cannot be coaxed to hold three or four ounces, and in some of these cases a catheter can be slipped into the ureter.

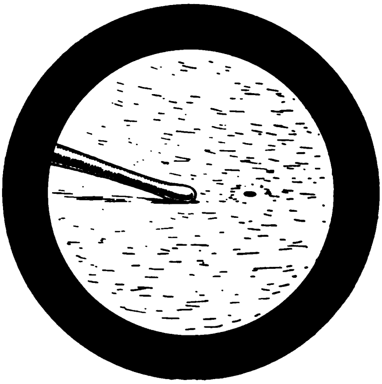

Fig. 34.—Catheter at rigid ureteral orifice.

There may be difficulty in finding the ureters. In a trabeculated bladder the interureteric bar may be lost among a maze of ridges, separated by deep clefts and hollows. The injection of indigo-carmine may be of assistance in the search for the ureteric openings. A puffy, inflamed mucous membrane may conceal the openings among its folds.

The ureter sometimes opens on the back of a prominent ridge, and, although visible, may be difficult of access with the ureteric catheter. The injection of a little more fluid into the bladder may assist the operation. I have met with one case in which the bladder base was infiltrated by old-standing inflammation, and the ureters opened as small immobile round holes in a rigid floor (Fig. 34). In this case I failed, after several attempts, to pass the catheter, being unable to get the tip into position to push it directly into the opening, or to pick up any fold at the ureteral mouth by sliding the catheter along the floor.

In another case the bladder was healthy, and there was no difficulty in entering the ureter with the point of the catheter, but on pushing the catheter onwards the mucous membrane became invaginated a little way, and then further progress was arrested. Both openings were too small to admit the finest catheter, although no disease was present in the bladder or ureters.

Patients occasionally complain of a colicky pain when the catheter is lying in the ureter. In a nervous man this amounted to renal colic, which subsided at once on withdrawing the catheter. In a few cases the presence of the catheters has occasioned some spasm of the bladder. A hot fomentation applied to the abdomen will promptly relieve the ureteric or vesical spasm, and it is seldom necessary to abandon the examination on this account.

The dangers of ureteric catheterisation are confined to infection of the ureter, kidney pelvis, and kidney.

Damage to the ureteric opening, causing ecchymosis and after-contraction, are alleged (Maitland) dangers of the method. This results from want of care on the part of the operator, and is not caused by the instruments at present in use unless the operation is performed in an unskilful and hasty manner. I have examined the ureteric orifices in many of my cases from three days to a week after the operation, and have seldom been able to detect any congestion or other change in the mucous membrane.

Infection of a healthy ureter or kidney by the introduction of a ureteric catheter is a danger about which much has been written. The infective material may be introduced upon the catheter from outside sources, or it may be derived from the bladder.

I have already discussed the method of sterilisation and preservation of the catheters. Constant care is required to keep these catheters smooth on the surface and clean outside and in, and unless this is exercised the surgeon is not justified in performing the operation. With proper care, there is no danger of introducing septic material into the ureter where the bladder is healthy.

My experience extends well over two hundred cases, and in none of these has infection followed the operation. Casper and Nitze, Albarran, Kalischer, Pasteau, Kelly, Kümmel, Tilden Brown, and many other surgeons of standing, speak from prolonged experience of the safety of this method of examination in skilled hands. On the other hand, a few cases have been recorded by Israel, Desnos,* and Legueu † to shew that infection may take place.

The danger of infecting the ureter and kidney by the ureteric catheter passing through an infected bladder would appear to be more imminent than the introduction of sepsis from without. This has been compared to the infection of the bladder by a catheter passing through an inflamed urethra. But the simile is not exact. The urethra is in contact with the whole length of the instrument, and there is a danger of pushing discharge before it into the bladder. The ureteric catheter, on the other hand, is only exposed for a very short distance between the internal opening of the tunnel in the catheter and the ureteric opening, and this passes through a fluid which is almost certainly sterile, for it is introduced into the bladder as such, after careful washing of the bladder.

Further, the ureteric catheter is not introduced as far as the pelvis of the kidney, but is only passed about 5 or 6 inches along the ureter. It may be said that bacteria can be carried upwards by retrograde currents of urine, and that the sphincter action at the lower end of the ureter may be temporarily destroyed and allow of the regurgitation of septic fluid into the ureter.

But it is recognised that the presence of bacteria alone in the urinary tract is not sufficient to cause inflammation.

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* Congrès d'Urologie, 1898.

† Congrès Internat. de Méd., Paris, 1900.

This has been proved experimentally by Albarran,* who injected pure cultures of virulent micro-organisms into the ureters and found that an ascending infection only occurred under certain predisposing conditions. And it is further known that tubercle bacilli are frequently (50 per cent.) present in the urine of consumptive patients,† being passed through the kidneys and urinary tract without causing tuberculous disease of these organs. Again, in the condition known as bacilluria myriads of bacteria render the urine opaque, and the urinary tract, with the exception of some small focus, remains healthy. Further, it will be generally admitted that the passage of instruments through infected strictured urethræ may be continued for years without arousing cystitis by infection. Two factors predispose to the development of inflammation where bacteria are at hand in the urinary tract—namely, injury and obstruction. Of these, only the first applies to catheterisation of the ureters. Delicacy of manipulation is therefore a point of the greatest importance in this operation.

If bacteria are introduced with the catheter into the ureter, they must be swept away by the urine, for the cases of cystitis in which the operation has been performed are many, and the records of infection of the kidneys are very few.

The problem is the same where one kidney is diseased, say with pyonephrosis, and the other healthy. In such a case the surgeon will usually content himself with catheterising the ureter of the diseased side, and if the bladder is free from disease, draining the viscus with a urethral catheter in order to obtain the urine of the second kidney.

But when cystitis is present the result obtained by this method will be open to criticism, for foreign material may be added to the urine of the second kidney by the walls of the inflamed bladder. In such a case, reliable information can only be obtained by catheterisation of the ureter of the sound kidney after careful washing of the bladder.

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* Thèse de Paris, 1889.

† Foulerton and Hillier, *Brit. Med. Journ.*, Sept. 21, 1901.

A somewhat similar problem will arise in regard to the catheterisation of the ureter in a case of tuberculous disease of one kidney where cystitis is present. It is usually assumed in such a case that the cystitis is tuberculous in nature, and that the catheter will carry bacilli from the bladder into the healthy ureter. But there are many of these cases that for a considerable period of time after the symptoms of cystitis have become established do not shew cystoscopically the appearances of tubercular cystitis. If the tuberculous kidney be removed the inflammation of the bladder disappears. In such cases the bladder is, I believe, non-tuberculous at this stage, and there is little or no danger of infecting the second kidney with the catheter.

In the case where the cystitis is actually tuberculous in nature and descending from one kidney, the area of tuberculous inflammation usually surrounds the ureteric orifice of the diseased kidney, leaving the rest of the bladder —or at least the neighbourhood of the second ureter—free from disease. The catheter does not search along the mucous membrane of the bladder and stir up tuberculous foci, but passes straight into the ureter without touching more than its lips. The danger of infection in these cases does not appear to me to be imminent.

Where the tuberculous disease of the bladder is widespread, and where the opening of the second ureter or its neighbourhood is involved, it is unlikely that catheterism of the ureters will be feasible, on account of the contracted irritable state of the bladder ; and attempts to carry it out in such a case are, I believe, unjustifiable.

Catheterisation of the ureters is not an operation to be undertaken without due consideration. The possibility of the dangers that I have discussed must be carefully weighed and against them must be placed the value of the information which it is hoped to obtain. One cannot look through the list of cases that I have collected (*see* Appendix) where tuberculous and other kidneys have been removed and the second kidney found to be absent, atrophied, or totally destroyed by disease, without feeling that a considerable risk would have been justified in order to obtain information the lack of which ended in operative disaster.

CHOICE OF AN INSTRUMENT FOR SEPARATION OF THE URINES

There are certain advantages and certain disadvantages in the use of each of the various instruments.

1. **Ease of application of the methods.**—The separator is more easily introduced, and thus appeals to a wider field of workers than the ureteral catheter.

Catheterisation of the ureters undoubtedly requires skill, experience, and patience, and the necessary delicacy of manipulation is not acquired without care and practice. A knowledge of cystoscopy is the groundwork upon which the operation rests. The method is thus unsuited for universal use, but it is open to many to acquire the necessary knowledge and technical skill.

I have not found the introduction of the separators invariably easy, and there are cases where the operation is attended with extreme difficulty. The instrument of Cathelin is more easily passed into the bladder than that of Luys. It cannot be said that experience in urinary surgery can be dispensed with in dealing with these instruments.

The decisions which depend upon the result of such an examination are too important to permit of their being drawn from a method imperfectly practised. If any doubt exists as to the accuracy of the separation, the examination is better left undone.

As I have elsewhere* pointed out, the use of the cystoscope is an indispensable preliminary to the separation of the urines by means of these instruments. The diagnosis between vesical and renal disease must first be established, and then the separator may be used. A case of hæmaturia unaccompanied by other symptoms may be taken as an illustration. A separation of the urines will only demonstrate unilateral hæmaturia, and there is nothing to shew whether it comes from the bladder or kidney unless the cystoscope is used. Mistakes are still more likely to occur where symptoms pointing to disease of one kidney accompany hæmaturia. A papilloma at one ureteric opening is frequently accompanied by pain in the corresponding kidney, although the kidney may be healthy. Intravesical separation of the urine in such a case will give unilateral hæmaturia on the side of the pain, and support the erroneous diagnosis. I have known the intravesical separation fail where there had been symptoms of calculus in one kidney, and the stones were actually lodged in the bladder and discovered by a subsequent cystoscopy.

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* *Practitioner*, June, 1905; and *Clin. Jour.*, Sept. 20, 1905.

It will be admitted, therefore, that a knowledge of cystoscopy is a necessary preparation for the use of the separator. The difference between the skill required for the two methods of separation is therefore much reduced. It is but a step from cystoscopy to ureteral catheterisation, and the method of cystoscopy plus intravesical separation of the urine is no more an operation for the multitude than is catheterisation of the ureters.

Another point which may sometimes weigh in the choice of a method is that two examinations are required for cystoscopy and intravesical separation, while one will suffice for cystoscopy and ureteral catheterisation.

2. **Danger of infecting the kidneys.**—A second advantage that is claimed for the intravesical separators is that there is no fear of infecting the kidneys by their use.

I have already discussed the question of renal infection by ureteral catheterisation when considering the dangers of this procedure. The danger of such an accident is, I believe, much overstated, and the testimony of many surgeons of standing gives support to this view.

In proper hands, infection of the renal pelvis and kidney is less to be feared than the infection of an operation wound, and much more has been heard of the matter than is justified by the evidence upon which it is based.

3. **Accuracy of separation.**—The object of the examination is to discover the composition of the urine as it is discharged from the ureter before blending with the secretion from the second kidney, and without being contaminated by the addition of foreign matter from the walls of the bladder. Both the ureteric catheter and the intravesical separator have given accurate results times without number. But there are also many cases where the accuracy of the division made by the intravesical separator is open to doubt. The separator is dependent upon the accurate and constant application of the instrument to the bladder base, and although this can be accomplished with precision where the bladder is healthy and in the female subject, it cannot always be relied upon where disease is present.

It is certain that a catheter passed into one ureter draws urine only from that kidney, and if both ureters are catheterised the separation of the urines is absolute and complete. The only fallacy is that some urine may trickle down the ureter alongside the catheter and escape into the bladder. This will not, however, contaminate the other urine, and the only effect will be to lessen by a very small amount the quantity of urine flowing from one catheter. This only happens on rare occasions, and I believe usually when a marked diuresis is in progress. It is prevented by passing the form of catheter used by Albarran and myself.

When the bladder has been proved healthy by the cystoscope, changes in the composition of the urines collected by a separator may be referred to the kidneys; but when the bladder is diseased no amount of washing will exclude the possibility of contamination of the urine by contact with the bladder wall before flowing from the catheters of the intravesical separator.

The urine which flows from the ureteral catheter may be tinged with blood from an abrasion of the mucous membrane of the ureter. If the catheter be pushed on a little way clear urine will flow.

The passage of the separator may give rise to an abrasion of the mucous membrane of the urethra at the entrance into the bladder and the urine is blood-stained. Accidental hæmaturia may therefore occur with either instrument.

4. **Duration of the examination.**—A disadvantage of the separator when compared with the ureteral catheter is that the time during which it can be borne by the patient is limited to about half an hour, and during this time the surgeon must be in constant attendance, and continually on the alert to keep the instrument accurately in place. The ureteric catheter, when once placed in position, may be left for some hours in the charge of a nurse or assistant who collects the urine and withdraws the instrument when the examination is at an end. The importance of this will become apparent when the tests for the function of each kidney are studied.

Of the two methods I prefer catheterisation of the ureters, and believe that more accurate results are obtained by this means.

In children the only available means of obtaining the unblended urines is by the child's separator of Luys.

CHAPTER V

EXAMINATION OF THE URINES OF THE TWO KIDNEYS

Variation in the Activity of Healthy Kidneys—Modification of the Function by the Use of the Separator or Catheter—Variation where one Kidney is Diseased—Cryoscopy of the Urines—Chemical Examination of the Urines

I.—WHERE BOTH KIDNEYS ARE HEALTHY

It is known, from the observation of series of cases, that the average quantity of urine secreted by the combined action of the two kidneys in a healthy individual amounts to from 1,200 to 1,700 c.c. in twenty-four hours, and that it has a specific gravity of from 1015 to 1025 and a freezing point of -1.30 to -2.30. The average composition is the following:—Urea, 30 grammes; uric acid, 0.8 gramme; phosphoric acid as phosphates, 3.5 grammes; hydrochloric acid as chlorides, 6 to 10 grammes.

With the separation of the urine into the output of each kidney the necessity for a new standard of comparison arose. It was not sufficient to divide the total output by two in order to indicate the work of one kidney, for Goll,* Ludwig,† Paulsen,‡ Landois,§ and others have shewn the unequal physiological value of the kidneys at a given time in animals.

Bardier and Frenkel|| (1899), Casper and Richter¶ (1901), Strauss** (1903), Kapsammer†† (1903), and

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* Inaug. Diss., Zürich, 1853.
† *Lehrbuch d. Physiologie*, 1861.
‡ Inaug. Diss., Kiel, 1891.
§ *Traité de Physiologie*, 1893.
|| *Jour. de physiol. et de pathol. gén.*, 1900, p. 413.
¶ "Nierendiagnostik," 1901, S. 83.
** *Berl. klin. Woch.*, 1903, S. 193.
†† *Wien. klin. Woch.*, No. li., 1903.

Albarran* (1904) have studied this question in the human subject. The earlier work appeared to shew that the conclusions of the physiologist did not apply to the function of the human kidney, and that each organ produced simultaneously a practically equal quantity of urine of similar composition.

More recently, independent observations by Kapsammer and Albarran in animals and in the human subject have led to conclusions different from those of the earlier workers. I shall here adopt their views.

The kidneys do not work simultaneously with the same energy, and the function of each varies at different parts of the day. There is no regular alternation between the secretion of the two kidneys, but when the total secretion of each kidney during 10 or 12 hours is examined it is found that the work is about the same.

One may consider as normal a kidney that secretes the following in 24 hours :—

Quantity . . .	600 to 700 c.c.
Urea	12 to 15 grammes.
Chlorides. . . .	5 to 6 grammes.
Δ	-1.30 to -1.50.

But when the urine of one kidney secreted during a shorter time is compared with that of the other kidney, a difference is found.

If the urine of each kidney be drawn separately for a quarter of an hour or half an hour, the difference in quantity may amount to from 10 to 30 per cent. By collecting the urines for three-quarters of an hour the difference may amount to 15 per cent., and for one hour it is reduced to 10 per cent.

The composition of the urines secreted also varies. In Albarran's observations the difference between the proportion of urea per litre secreted by the two kidneys amounted to 1 gramme in 25 per cent. of cases, and might reach 6.45 grammes. The actual quantity of urea secreted in a quarter of an hour and measured in centigrammes shewed less difference, for the urine which was greatest in quantity was less concentrated. The difference in the quantity of urea secreted by each kidney was less where the time of collection was more extended.

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* *Annales des malad. des organ. génito-urin.*, 1904, p. 82.

The chlorides secreted by each kidney shewed a difference in quantity, which did not usually rise above 1 gramme per litre, but occasionally almost reached 5 grammes per litre. Here also the salt was more concentrated in the urine which was secreted in less quantity. When the quantity of urine secreted by each kidney was equal there was little difference in the chloride content. When the urines were collected during a long period of time the chloride content became equal. Differences in the quantity of phosphates secreted by each kidney followed, in a general way, the variations in urea and chlorides, but were less marked.

The secretion of urine by a healthy kidney may be modified by the passage of the instruments necessary for the separate collection of a sample from each kidney. Immediately after the passage of a ureteric catheter there may be a pause in the renal activity for a minute or so. It has very rarely lasted 10 minutes in a healthy kidney. This temporary anuria is followed by a period of oliguria, and then the normal secretion is re-established. A similar effect has been observed in the use of the urine separators by Schüller,* Rafin,† Keydel,‡ and others.

Kapsammer has pointed out that a polyuria not infrequently follows the passage of the ureteric catheter. The instrument appears to act as an irritant, in the same way as a calculus in the renal pelvis, and causes an increased flow of urine. If the kidneys are healthy this polyuria is bilateral. Albarran found that polyuria followed the introduction of a catheter into the ureter in 41 per cent. of healthy individuals. In over 52 per cent. there was no departure from the normal secretion.

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* *Wien. klin. Woch.*, 1904.

† "Travaux Cliniques de Chirurgie Urinaire," Lyon, 1904.

‡ *Centralbl. für die Krankh. der Harn. u. sex. Org.*, 1905.

II.—WHEN ONE KIDNEY IS DISEASED

1. **Modification of function due to the examination.**—The passage of a ureteric catheter may reflexly affect the secretion of a diseased kidney or its healthy neighbour in the same manner that has been noted in the case of two healthy organs. Oliguria, which sometimes results, is very rarely either of severe degree or long duration.

Albarran found that oliguria more often followed the passage of the intravesical separator (45 per cent.) than of the ureteric catheter (8 per cent.). This is probably to be explained by the fact that the examination by the separators was of short duration—about 20 minutes—and it is during the first quarter of an hour that oliguria is observed. The examinations by the ureteric catheter, on the other hand, were prolonged for several hours, and the initial oliguria, if it occurred, would have passed off and might be followed by polyuria.

Polyuria may result from the irritation of the catheter, and, according to Kapsammer, is only seen on the side on which the ureteric catheter lies, if only one be passed. Albarran does not, however, agree that the polyuria is unilateral unless where one kidney is completely destroyed by disease. An initial polyuria was observed by Albarran more frequently with ureteric catheterisation (22 per cent.) than with the use of the separator (16 per cent.)

It will be seen, therefore, that a temporary modification may be observed in the quantity of urine secreted. The variation is principally in the quantity of water, and the other urinary constituents vary but little. The modifications are not so marked as to reduce the value of the information gained by these methods. It is evident that examinations extending over a short period of time such as 15 or 20 minutes are likely to give fallacious results, while more prolonged drainage of each ureter gives greater accuracy.

2. **Changes in urine due to disease.**—(*a*) *Changes in quantity of each urine.* A diseased kidney usually secretes less urine than its healthy or less diseased neighbour. This will to some extent depend upon the form and extent of the disease. A hydronephrotic kidney will pass no urine through the catheter, or a very small quantity, when the ureteral block is complete or nearly so. The following cases illustrate these remarks.

Mrs. S. was sent to me by Dr. Chearnley Smith, of Worcester Park, complaining of uneasiness and swelling in the left loin. There had been one attack of severe pain in the left renal region some months before I saw her. There was a large painless tumour occupying the position of the left kidney. The vesical orifice of the left ureter was thick-lipped and round, and an occasional feeble ureteral contraction was seen, but no efflux. The right ureteric orifice was large, oval, and its thin lips were translucent. It shewed pronounced contractions. The right ureter passed 158.5 c.c. of urine in two hours after the administration of a diuretic. The urine contained 1.3 per cent. of urea. The left ureter passed no urine. On operation, a large hydronephrosis was found with complete blocking at the uretero-pelvic junction.

In a second case (G. J.), a man aged 42, there was a similar condition of the right kidney. The right ureteric opening was oval and thick-lipped, the left small and healthy. The ureteric catheter drew no urine from the right ureter; the left ureter passed 150 c.c. of urine, containing 2 per cent. of urea, in two hours.

In another case of less advanced hydronephrosis (H. D.), where the block was apparently due to stenosis at the uretero-pelvic junction, the dilated kidney secreted 45 c.c. of urine and the healthy kidney 213 c.c. in two hours after the administration of a diuretic. In one case (J. V.)

of calculous pyelonephritis and pyonephrosis, where the kidney substance was small in amount and tough and hard in consistence, and the kidney contained a collection of small calculi, masses of putty-like pus were expressed from the ureter, and the catheter drained no urine from this side. The second kidney secreted 435 c.c. of urine during two hours after the administration of a diuretic.

In a case of calculous pyonephrosis (F. L.) the urine drawn from the diseased kidney was small in amount, and contained large quantities of pus. Operation shewed numerous calculi, and a thick wall of somewhat fibrous kidney tissue surrounded the cavities containing them.

A patient (H.), from whose left kidney I removed three small stones, had septic and stinking urine, with a small amount of pus. From the diseased kidney 226 c.c. of urine was obtained, and from the healthy right kidney 222.5 c.c., a practically equal quantity.

On the other hand, an *increased quantity of urine* may be discharged by the ureter on the affected side. This is observed in some cases where the kidney is but slightly, if at all, diseased, and it appears to result from an increased activity in the circulation of the kidney.

In a man (C. L.) of 28 years, with a small oxalate stone in the left renal pelvis, the left kidney secreted 264 c.c. while the right kidney secreted 202 c.c. The kidney substance was found to be healthy at the operation.

In some cases of movable kidney a similar polyuria on the side of the affected organ is observed. A woman (E. W.), aged 29, was sent to me by Dr. John Lawrie, of Woking, with a movable right kidney without hydronephrosis. The movable kidney secreted 82.6 c.c., while the normal kidney secreted 68.4 c.c. of urine.

Polyuria of a different origin may be observed from a kidney the seat of advanced disease. In such cases the polyuria is due to interstitial nephritis caused by the surgical disease.

In a man (K.) with advanced tuberculous disease of the right kidney, the diseased kidney secreted 71.2 c.c., while the healthy left kidney secreted 65.7 c.c. In a case of calculous pyonephrosis of the right side (Mrs. J.), to which I shall refer more fully later, the diseased kidney secreted 206.5 c.c. and the healthy organ 107.5 c.c.

The polyuria of a diseased kidney is due to an increase in the water of the urine, but there is no corresponding increase in the other urinary constituents.

A healthy or slightly diseased second kidney usually secretes a greater quantity of urine than its diseased neighbour.

There may be an actual *polyuria on the healthy side*, and where this is present there is also an increase in the quantity of organic and inorganic constituents of the urine of this side.

In advanced lesions of one kidney the polyuria on the healthy side may be considerable. On the other hand, the quantity secreted by each kidney may be equal, but the urine from the sound kidney has a higher specific gravity, and contains a greater quantity of urea and phosphates.

(b) Changes in the naked-eye characters and specific gravity of each urine.—Where polyuria is present on one or other side, the urine of that side will be paler than that of the other. But apart from an increase in the quantity, the urine of the diseased side is not infrequently lacking in pigment, so that it is visibly paler than the secretion from the healthy organ. The admixture of pus or blood with the urine of the diseased kidney may be noted. The specimens should be centrifugalised, and a careful microscopical examination made for blood or pus cells, tube casts or epithelium, crystals or other formed matter.

The specific gravity will vary according to the concentration of the urine. In a case of calculous pyonephrosis, the analysis of the urines of which is given on page 246, the urine on the diseased side shewed a specific gravity of 1004 compared with 1011 on the healthy side. There was polyuria of the diseased kidney.

It is necessary to compare the specific gravity with the volume of urine passed before drawing conclusions. A small quantity of urine of low specific gravity is a sign of a poorly performed renal function, but a urine which is abundant in quantity and has a low specific gravity may be present either in a seriously diseased kidney or in a healthy kidney. Where the quantity is large and the specific gravity high, the renal function is well performed.

(*c*) *Cryoscopy of the two urines.* — Changes in the freezing point of the urine of each kidney depend upon an increase or decrease in the molecular content of the urines. The method of estimating the freezing point and the factors upon which variations in the freezing point depend have been fully discussed in considering the combined function of the kidneys. Where it is desired to estimate the functional value of one kidney by this means, the same restrictions and fallacies must be considered that have already been shewn to vitiate the results of the method applied to the combined function of both kidneys. Just as in estimating the total function of the kidneys the volume of urine and its molecular composition change under varying conditions of food, drink, exercise, bodily temperature, etc., and during the day and night, so the composition of a single kidney urine will change. Thus it becomes necessary to collect the urines by catheters during 24 hours, and to examine the specimens thus obtained; and the observation to be of value must be repeated on several successive days, and under a carefully regulated regimen of food and drink. It is evident that such a method of examination is impracticable, and observations can only be made, if cryoscopy is to be used, upon urines secreted during a much shorter period of time (two or three hours). The variations in healthy individuals, even with a careful control of the solid and fluid intake, are very considerable, and I do not believe that any trustworthy data in regard to the functional activity of one kidney can be obtained by this method.

Comparative cryoscopy of the two urines will, however, give some information in regard to the difference of function between the two kidneys, and, if it has been ascertained by other means that one of them is healthy, the secretion of this may act as a standard for comparison.

It is necessary to know the quantity of urine secreted by the kidneys in a given time if the results of cryoscopy are to be of any value. Usually there is a diminished quantity of urine, with a reduced molecular content, and therefore a lowered freezing point, on the diseased side.

Where there is polyuria on the diseased side the freezing point will be still further lowered.

Polyuria on the sound side will lower the freezing point on this side, so that the diseased kidney may secrete a urine of greater molecular concentration, and thus appear to be the more active organ of the two.

When the volume of urine from one kidney is greater and the freezing point is higher, shewing a greater molecular content, this kidney is functionally more active than its neighbour.

In the less advanced stages of renal disease the cryoscopy figures are not usually altered, but, where disease has destroyed a large part of a kidney, there is usually a marked difference between the freezing points of the two urines. The urine of the diseased side will shew a lowered freezing point, while that of the healthy side will have a normal freezing point.

Kümmell* gives the following figures of the cryoscopy in three cases of pyelonephritis :—

Diseased kidney.	*Healthy kidney.*
— 0.19	— 1.75
— 0.13	— 1.03
— 0.37	— 1.53

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* XIII. Congrès International de Médecine, Paris, 1900.

The variations in the freezing point of the urine do not follow closely fluctuations in the quantity of urea, sodium chloride, and phosphates.

(*d*) *Estimation of urea, sodium chloride, and phosphates.*—In dealing with the estimation of the urea in the blended urine of both kidneys, I pointed out the fallacies that underlie this method of estimating the function of the kidneys. Even where a mixed sample of 24 hours is examined there are many extrarenal causes for variation in the quantity of urea excreted.

Where it is desired to estimate the function of one kidney the urine secreted during a short period of one or two hours must suffice, since more prolonged catheterisation as a routine measure is inadvisable. The likelihood of fallacy is therefore greater here than in the examination of the whole urine of both kidneys.

As a means of comparing the function of the two kidneys in a given time, however, the examination has some value.

The percentage of urea in the urine of the diseased kidney is reduced, and the difference between this and the quantity in the urine of the healthy kidney may amount to 1 per cent. or even more.

In a case of calculous disease of the left kidney (Mr. H.) where several small calculi occupied the calyces of a moderately dilated kidney and the urine was foul-smelling, the urea was estimated in six samples, taken at regular intervals during two hours, with the following results:—

	Left kidney (diseased). *Urea.*		*Right kidney (healthy).* *Urea.*
	0.75 per cent.		1.7 per cent.
	0.88 ,,		1.75 ,,
	0.7 ,,		1.75 ,,
Polyuria from diuretic	0.6 ,,	Polyuria from diuretic	1.1 ,,
	0.45 ,,		0.55 ,,
	0.3 ,,		0.8 ,,

In a case of advanced tuberculous disease of the right kidney (K.) an even more striking difference was observed.

Right kidney (tuberculous). *Urea.*	*Left kidney (healthy).* *Urea.*
0.9 per cent.	2.4 per cent.
1.1 ,,	2.4 ,,
1.0 ,,	2.6 ,,
0.8 ,,	2.5 ,,

In a case of hydronephrosis (Mrs. D.) where the kidney was dilated and the pockets contained masses of old blood clot, the following was the result of eight examinations made in 2½ hours :—

Left kidney (movable and dilated). *Urea.*	*Right kidney (healthy).* *Urea.*
0.45 per cent.	1.4 per cent.
0.55 ,,	1.5 ,,
0.68 ,,	0.93 ,,
0.45 ,,	0.89 ,,
0.49 ,,	0.9 ,,
0.5 ,,	1.0 ,,
0.6 ,,	1.0 ,,
0.55 ,,	1.0 ,,

The diminution in the excretion of urea on the diseased side appeared to depend upon the extent of the destruction of kidney tissue, for, in cases where the disease was less advanced, little or no difference could be detected in the amount of urea in the urine of the two sides.

Polyuria on the side of the healthy kidney may reduce the percentage of urea below that of the diseased side.

A young man (H. B.) suffering from early tuberculosis of the left kidney had a polyuria on the healthy right side, and the percentage of urea was less on this than on the diseased side on several examinations.

Right kidney (healthy).		*Left kidney (tuberculous).*	
Urea.	*Urine.*	*Urea.*	*Urine.*
0.4 per cent.	47 c.c.	0.4 per cent.	39 c.c.
0.15 ,,	91 ,,	0.3 ,,	26 ,,
0.2 ,,	94 ,,	0.45 ,,	29 ,,
0.25 ,,	33 ,,	0.45 ,,	24 ,,
0.8 ,,	21 ,,	0.51 ,,	10 ,,

On the other hand, polyuria on the diseased side may still further reduce an already diminished urea percentage.

The following figures were obtained in the case of Mrs. J., who suffered from right calculous pyonephrosis:—

Right kidney (*pyonephrosis*).		*Left kidney* (*healthy*).	
Urea.	*Urine.*	*Urea.*	*Urine.*
0.4 per cent.	206.5 c.c.	1.3 per cent.	107.5 c.c.

The actual quantity of urea eliminated in a given time should be estimated. A normal kidney should secrete 1.2 to 1.8 grammes of urea in two hours. A moderate elimination in this time would be 0.75 grammes to 1.0 grammes, but the function is poor where the urea is reduced below 0.75 grammes.

Variations in the elimination of sodium chloride and phosphates follow those of urea. Sodium chloride is diminished on the side of the diseased kidney, but it is apparently more easily excreted by a diseased kidney than is urea, for the variations in quantity are less. Sodium chloride has been found equal in quantity on the two sides and even in excess on the diseased side. Albarran and Kapsammer have observed unilateral phosphaturia, and the latter observer has found phosphaturia on the diseased side in a case of renal tuberculosis.

CHAPTER VI

TESTS FOR THE FUNCTIONAL ACTIVITY OF EACH KIDNEY

Methylene Blue Test—Indigo-carmine Test—Phloridzin Glycosuria Test—Albarran's Experimental Polyuria Test—Practical Application of the Methods of Estimating the Functional Activity of the Kidneys

1. **Methylene blue test for each kidney.**—In 1897 Guyon and Albarran* published observations upon the use of methylene blue, combined with catheterisation of the ureters, for the estimation of the function of one kidney. In a further publication Albarran and Bernard † elaborated these observations by the investigation of a further series of cases.

The injection is made in the manner already described, and the time of appearance, duration, and depth of staining of the urine are the same as those noted for the combined function (page 84). The blue is eliminated poorly by a diseased kidney. It appears later, colours the urine less deeply, and its duration may either be prolonged or shortened. There may be a delay of one or even three hours before the appearance of the blue staining of the urine of the diseased kidney, and after a feeble coloration for twenty-four hours it may completely disappear. The chromogen may be more abundant than the blue.

Chart 26 shews the elimination of methylene blue and chromogen by each kidney in a case of hydronephrosis. On the healthy side a normal elimination of blue of four days' duration is seen. The hydronephrotic kidney passed blue-stained urine in three hours after the injection, and the urine was feebly coloured for three days. Chromogen appeared in six hours, and was more abundant than the blue.

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* Assoc. franç. d'urologie, 1897.

† *Annales des malad. des org. génito-urin.*, 1898, p. 237.

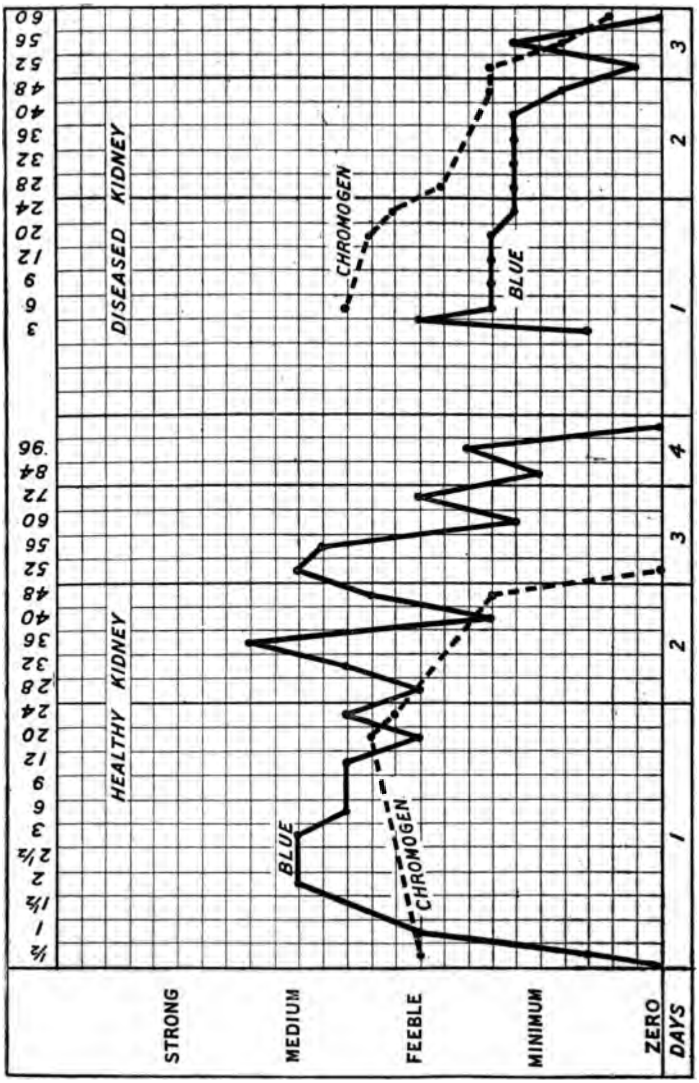

Chart 26.—Elimination of methylene blue and chromogen in a case of hydronephrosis. Delay and diminished quantity of blue and delay of chromogen on diseased side (Albarran).

In using methylene blue as a test of the function of each kidney, it is obviously inadvisable to make observations as a routine measure for the sixty or more hours during which the blue may be expected to be present in the normal state. Still less is it expedient to attempt the drainage of each kidney during the protracted elimination that frequently occurs in disease.

Two of the important points in the elimination of methylene blue by the kidneys may, however, be investigated with a comparatively short ureteral drainage. Observations may be made on the time of appearance of the blue and chromogen, and the depth of staining of the urine as a measure of the quantity of blue eliminated. For this purpose a catheterisation of an hour, or at most two hours, will suffice. I have selected the following cases from my note-books, as they indicate the extent of the information that may be gained by this method, and shew how far the conclusions based upon it were justified.

Case 1.—F. C., a man suffering from right-sided pyelonephritis of ten months' duration, with an enlarged tender kidney. On the right (diseased) side methylene blue appeared in the urine in 60 minutes as a dirty green coloration, and the microscope shewed pus and renal cells and bacilli. The left ureter gave clear blue urine in 30 minutes after the injection, and this became deeply stained. Nephrotomy was performed on the right side, and the symptoms subsided.

Case 2.—F. L., aged 48, came under my observation at the North-West London Hospital. There was a large, hard left kidney, the right kidney was not palpable or tender. The urine from the left kidney was purulent, and contained 1½ grammes of urea per litre. No methylene blue and no chromogen appeared in the urine on the left side. The right urine was deeply stained with methylene blue, and chromogen was present in quantity 27 minutes after the injection. A large multilocular pyonephrotic cyst, with thin fibrous walls and containing masses of calculi, was removed from the left side (Plate VIII.). The wound was soiled with pus, and the patient died with symptoms of septic absorption. The remaining kidney (right) was found to be healthy.

Case 3.—R. S., a man aged 46, attended my out-patient department at St. Peter's Hospital suffering from renal calculus. There was pain in both kidneys. A large, hard, irregular mass was felt in the situation of the right kidney. The left kidney was not palpable or tender. There were no symptoms of renal failure, except constant thirst. No blue or chromogen appeared in the urine of either kidney. Operation was refused, and the patient died of suppression of urine 18 months later. The left kidney was also destroyed by calculi.

Case 4.—Mrs. J., aged 35, gave a history of hæmaturia since childhood. There had been intermittent pain in the right kidney and groin, and she had undergone an operation for supposed appendicitis. The right kidney was moderately enlarged. It passed no blue, but a small amount of chromogen appeared. The left kidney passed chromogen in quantity in 25 minutes after the injection, and blue in 1 hour 50 minutes. The right kidney was found on operation to contain large calculous masses, with a thin covering of fibrous renal tissue. The patient made a good recovery after nephrectomy.

In my cases where surgical interference was proposed in disease of one kidney, an early onset of elimination and a good quantity of blue in the urine were accepted as a guarantee of the functional activity of the second kidney, whereas the absence of blue and chromogen in the urine of the second kidney was taken as an indication of an inefficient or destroyed kidney.

Between the extremes of a well-marked blue elimination and its complete absence from the urine of the second kidney, there are varying degrees. In these cases it is

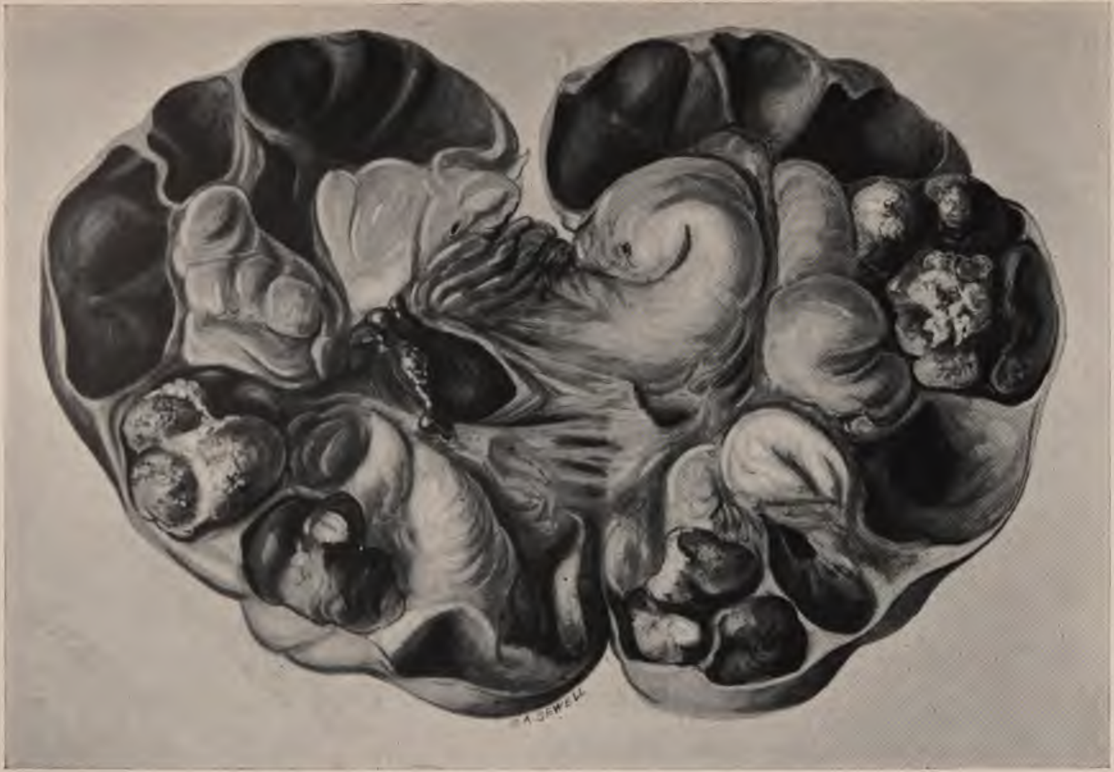

Plate VIII.—Calculous pyonephrosis. Nephrectomy.

impossible to lay down strict rules for guidance in regard to the estimation of the functional activity of the kidney; what may be considered a satisfactory elimination of blue, and what a serious deficiency, becomes a matter of experience.

In making observations upon such cases the methylene blue method suffers from the disadvantage of a long duration. The drainage of each ureter by catheter during a period of two or three days is impracticable as a routine measure. It is, therefore, impossible to note the duration and course of the elimination or to estimate the total quantity of blue eliminated.

Except in such pronounced results as those I have related, the method does not provide sufficiently definite information on which to base conclusions as to the total function of one kidney. But, as a means of comparing the work of the two kidneys in a given time, it has an undoubted value.

If the combined function of the kidneys is estimated at a high value by any of the methods which have been described in the earlier part of this work, and if the separation of the urines shews that the blue is eliminated with little delay on either side and in about equal quantity, the active renal tissue is probably distributed pretty evenly between the two organs, and is present in good quantity. If, on the other hand, the combined function of the kidneys is found to be considerably reduced, and, by draining each kidney, the proportion of blue is found evenly distributed between the two, it would be inferred that a diminished amount of renal tissue was distributed equally between the two organs, and for this reason nephrectomy might be contra-indicated.

When the difference between the two secretions is so marked that the supposed healthy kidney eliminates much the greater quantity of methylene blue, it will appear probable that this kidney has already assumed a large part of the renal function, and may be trusted to carry it on if the diseased organ is removed. This demonstration of the renal function will be the more striking if the diseased kidney eliminates no trace of blue or chromogen.

On the other hand, it is certain that if the second kidney is the seat of latent disease which has hitherto passed unnoticed, examination of the urine drawn by catheter from that ureter will give a clue to the presence of the disease, which will be strengthened by the use of the methylene blue test.

In the lesser grades of surgical renal disease no difference may be noticed between the two sides in the elimination of methylene blue. Thus, in a case of movable kidney with slight hollowing of the kidney, methylene blue was eliminated in good quantity by each kidney half an hour after an intramuscular injection.

I have not observed, as a frequent occurrence, the intermittent elimination of methylene blue by the healthy second kidney which Albarran attributes to compensatory hypertrophy.

Where one kidney is diseased and the other healthy, or almost so, the function of the latter may be adversely influenced by the presence of the diseased kidney—a reno-renal depressant reflex. This depressant effect influences the elimination of methylene blue by the healthy or less diseased kidney, and may abolish it altogether.

The following observation illustrates this point: A stout, flabby man (J. R.) suffering from stricture and a large pyonephrosis came under my care. Twelve days after nephrotomy an injection of methylene blue was given. No blue appeared in the urine passed from the bladder, and none was found in the urine passing by the wound in the loin. Chromogen was found in the urine 1¼ hours after the injection, and rose to a deep green colour, lasting 48 hours altogether. Fourteen days after the nephrotomy I performed nephrectomy.

Injection of blue after the second operation shewed a marked improvement in the function of the remaining kidney. Chromogen appeared one hour after the injection and blue in 1½ hours. The urine was deeply stained for 28 hours. The excretion of chromogen was intermittent. It was present in greater quantity than the blue, and disappeared with it in 28 hours, reappearing for a few hours in 40 hours (Chart 19, page 117).

2. **Indigo-carmine test for each kidney.**—The injection of indigo-carmine was originally introduced by Völcker and Joseph as a substitute for catheterisation of the ureters, and this method has already been described under the name of chromocystoscopy (page 174). At a later date Völcker * combined the method with catheterisation of the ureters, and Kapsammer † has also recommended its use.

Twenty cubic centimetres of an aqueous solution of indigo-carmine (0.4 per cent.) are injected into the gluteal muscles, and observations are made upon the time of appearance of the dye in the urine and the depth of staining. I have not found that the method possesses any advantage over the methylene blue test. Only the time of onset and the depth of staining can be observed in either method, for the duration of each is too great to allow of catheterisation of the ureters during the whole period of elimination. It has been claimed as an advantage of indigo-carmine that no colourless derivatives are formed which may escape detection in the urine. The elimination of part of the methylene blue as a leuco-derivative is no great disadvantage so long as its existence is known, and the colourless body transformed into blue by acetic acid and heat. The large quantity of indigo-carmine that must be injected in order to get a well-stained urine is a disadvantage.

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* "Diagnose der chirurgischen Nierenkrankungen unter Verwerthung der Chromokystoskopie," Wiesbaden, 1906.

† "Nierendiagnostik und Nierenchirurgie," 1907.

Indigo-carmine is completely soluble in water up to the strength of 1 in 150, and a solution of this density may be used.* I injected 15 minims of this solution into the muscles of the thigh in a case of tuberculous left kidney. On the diseased side no staining of the urine with the dye occurred. On the healthy side the urine was stained a faint green in 19 minutes, and remained greenish in hue for about an hour. Nephrectomy was successfully performed. The quantity of indigo-carmine used in this case was too small.

3. **Phloridzin glycosuria test for each kidney.**—This test was first combined with ureteric catheterisation by Casper and Richter,† who estimated the percentage of sugar which appeared in the urine of each kidney after the hypodermic injection of phloridzin. It was found necessary, however (Pugnat and Revilliod‡), to measure the entire quantity of sugar which appeared in the urines, for variation in the quantities of urine introduced certain fallacies in the percentage. Kapsammer§ shewed that the time of appearance of the sugar in the urine was of importance, a delay taking place when disease of the kidney was present. The quantity of phloridzin injected and other points in the technique are the same as those already described (page 132).

I found it convenient for the purposes of comparison to collect the urine every quarter of an hour during the first hour and every half-hour after this.

With an injection of 5 mgr. of phloridzin the whole glycosuria had usually ceased in two hours; rarely it continued for another half-hour or an extra hour. In these tests the percentage of sugar and of urea, and the quantity of urine at the end of each quarter- or half-hourly period, was estimated; a chart of these was constructed and was found to be a ready method of demonstration and comparison. In addition, the absolute quantity of sugar eliminated by each kidney was noted.

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* Messrs. Allen and Hanburys were at some pains to ascertain the solubility of this body, and prepared sterile solutions for me.

† "Functionelle Nierendiagnostik," 1901.

‡ *Archiv. sen. de méd.*, 1902.

§ *Wien. klin. Woch.*, 1904.

In healthy individuals the elimination of glucose by the two kidneys is equal and parallel. Variations in the work of the two organs occur, however, which may amount to from 10 to 20 per cent. I have observed a difference of 0.45 gramme between the amount eliminated by each kidney (1.20 right and 1.65 left) in a healthy individual.

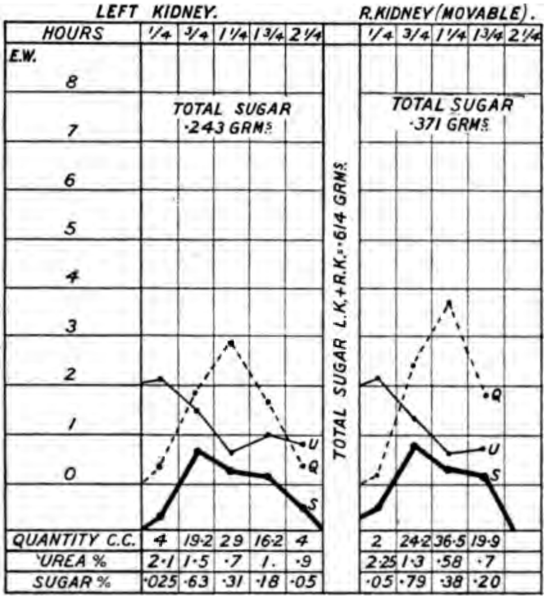

Chart 27.—Case of movable kidney. Elimination of sugar greater on diseased side. S represents sugar, U urea, and Q quantity of urine.

Albarran gives the following results in four healthy subjects :—

	Right Kidney.	*Left Kidney.*
1.	0.86 gramme.	0.68 gramme.
2.	1.20 ,,	1.14 ,,
3.	1.66 ,,	1.21 ,,
4.	1.80 ,,	1.62 ..

The elimination of sugar commences in a healthy kidney in the first half-hour, and most frequently the first appearance of it is observed in from 15 to 20 minutes after the injection.

The kidneys commence to eliminate the sugar simultaneously and cease almost at the same time. With an injection of 5 mgr., sugar is present in the urine for one and a half to two hours, and rarely for two and a half hours.

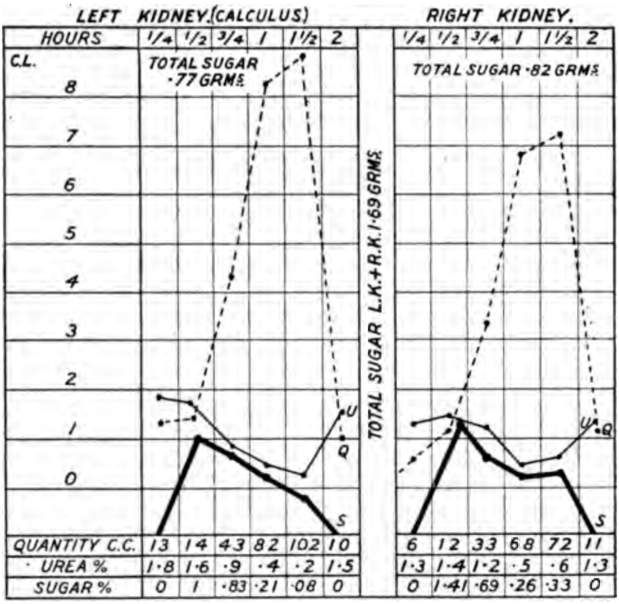

Chart 28.—Calculus of left renal pelvis. Elimination of sugar practically equal on two sides.

The curve of elimination rises to its height about three-quarters to one hour after the injection.

In the slighter grades of kidney disease the elimination of sugar on each side may be equal and parallel. Chart 27 is a record of the glycosuria and percentage of urea in each urine in a case of movable kidney. The glycosuria was slightly greater on the side of the movable kidney (.371 gramme right and .243 gramme left). The next chart (Chart 28) shews the glycosuria where a small calculus lay in the left renal pelvis. The sugar was slightly less in quantity on the left side (.77 gramme left and .82 gramme right).

With more advanced disease of the kidney the glycosuria is less abundant on the side of the diseased kidney. In a case of right calculous pyonephrosis .395 gramme of sugar appeared on the diseased side and 1.623 grammes on the healthy side (Chart 29).

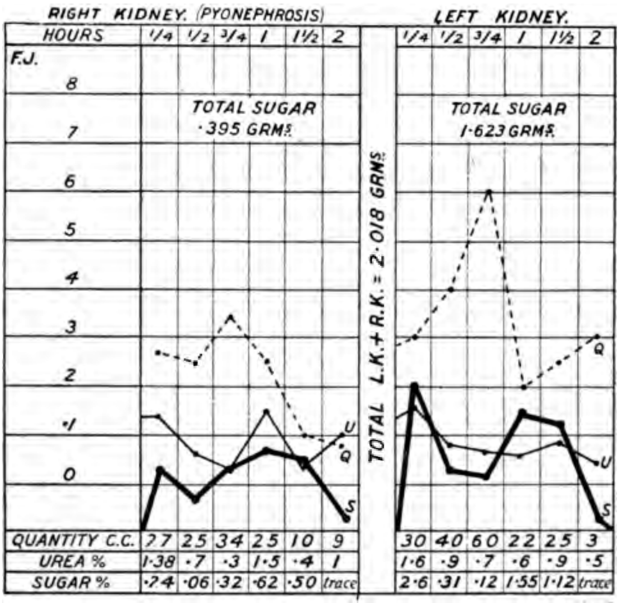

Chart 29.—Calculous pyonephrosis. Diminished elimination of sugar on diseased side.

This case may be shortly related, as it illustrates the value of this and other methods of estimation of the renal function, and shews the condition of the kidney examined.

Mrs. F. J., aged 35, came under my observation at the North-West London Hospital, in December, 1906. She gave a history of hæmaturia and right renal colic as a child of five years, and the occasional appearance of blood in the urine after unusual exertion from time to time since.

There had been pain across the back, more severe on the right side. A stone was passed in 1905. She had undergone an operation for appendicitis in a London hospital in 1903, but "no abscess was found." When I examined her the right kidney was enlarged and tender. The urine was milky with pus, with a specific gravity of 1014, and contained 1 per cent. of urea in a daily secretion of 20 ounces.

The following is the analysis of the separated urines :—

	Right kidney (diseased).	*Left kidney.*
Quantity	206.5 c.c.	107.5 c.c.
Specific gravity	1004	1011
Δ	—0.18° C.	—0.76° C.
Colour	Pale limpid	Fairly coloured
Urea	0.4 per cent.	1.3 per cent.
Uric acid	0.0067 ,,	0.0150 ,,
Chlorides as chlorine	0.09777 ,,	0.1112 ,,
Phosphates as P_2O_5	0.08 ,,	0.034 ,,
Methylene blue	No change in colour	Appeared 1 hour 50 minutes, green colour, duration 18 hours
Chromogen	Appeared 25 minutes, faint green	Appeared 25 minutes, deep green
Phloridzin glycosuria	0.395 grammes	1.623 grammes

A skiagram taken for me by Dr. Reginald Morton shewed large masses of calculi in the right kidney, and there were no shadows in the left renal area (Plate V., facing page 149).

After nephrectomy the patient made an uninterrupted recovery. The kidney (see *frontispiece*) was a shell containing large masses of calculi, which corresponded in size, shape, and number with those in the skiagram. A narrow margin of somewhat fibrous kidney tissue formed the wall of the sac.

It is interesting to note that the average quantity of urine for 9 days before the operation was 25.5 ounces, with a specific gravity of 1010 to 1012, and urea content of .8 to 1 per cent., and that for 9 days after the first week following the operation the average quantity of urine was 42 ounces, with a specific gravity of 1010 to 1015, and urea content of 1.4 to 2.2; and that this increased activity of the remaining kidney was maintained during 5 weeks' residence in the hospital.

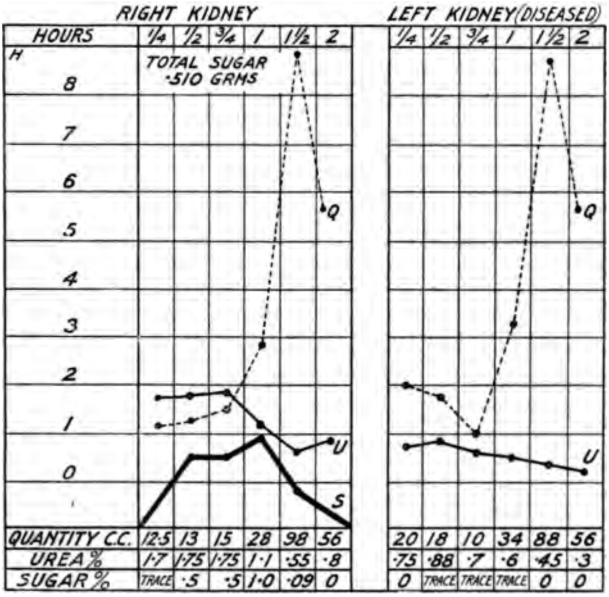

Chart 30.—Calculous hydronephrosis (Mr. H.). Traces of sugar on diseased side.

In several cases of advanced disease of one kidney sugar was present only in traces or entirely absent on the diseased side, and present in reduced quantity on the healthy side.

The following is the outline of such a case. I was asked to examine Mr. H., aged 44, by Dr. F. W. Collinson, of Preston. There was a history of attacks of left renal colic 14 years, 3½ years, and 6 months before I saw him, and there had been recent attacks. The urine had a penetrating, disagreeable, fishy smell for 6 months. There were no symptoms of renal failure. The left kidney was tender, but not enlarged. The ureters were catheterised and 5 mgr. of phloridzin injected. The accompanying chart shews the result of the examination (Chart 30).

On the left side traces of sugar appeared during three-quarters of an hour, and the urea varied from .3 to .8 per cent. On the right side .510 gramme of sugar was eliminated, and the urea varied from .5 to 1.7 per cent. On cutting upon the left kidney a dilated kidney was found filled with stinking but only slightly purulent urine, and three small stones were removed. The patient made an uninterrupted recovery.

A second case was under the care of my colleague, Mr. Freyer, in whose absence it fell to me to examine the bladder, and he kindly permitted me to make further observations in regard to the renal function.

The patient (K.) was a seafaring man of 54 years. He gave a history of frequent micturition during the day and night, and scalding during the act for some months. There had never been hæmaturia. The kidneys were not tender or painful, and neither kidney could be felt under deep anæsthesia. Tubercle bacilli were detected in the urine. Vesical spasm rendered cystoscopy difficult. The bladder shewed general subacute cystitis; the opening of the right ureter was far out on the side wall of the bladder; a thickened interureteral bar led up and into a tunnel which represented the ureteric opening ("dragged-out" ureter). Palpation of the kidney region of this side produced a powerful tug on this muscular ridge from contraction of the ureter. I catheterised the right ureter, drained the bladder with a small urethral catheter, and injected five milligrammes of phloridzin. No sugar appeared in the urine collected from the right ureter, and the urea varied from 0.8 to 1.0 per cent. The urine from the left kidney contained 0.296 gramme of sugar, and the urea varied from 2.4 to 2.6 per cent. (Chart 31). I diagnosed a functionless tuberculous kidney. On operation the right kidney was found to be destroyed by masses of caseous tuberculous material, and the ureter much thickened.

The following cases are three examples of the work of a solitary kidney after nephrectomy.

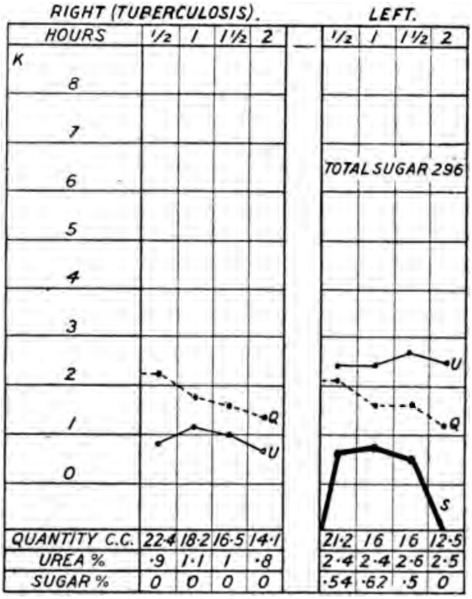

Chart 31.—Tuberculous right kidney. Absence of phloridzin glycosuria on diseased side.

In a patient (C. B.) whose right kidney I had removed 18 months previously for tuberculous disease, the remaining kidney eliminated 1.27 grammes of sugar, commencing 15 minutes after an injection of 5 mgr. of phloridzin and lasting 3½ hours (*see* Chart 24, page 141). The patient was in good health. In a second case (R.) of solitary kidney after nephrectomy no sugar was eliminated. I had removed a large pyonephrosis some months before, the operation having been followed by symptoms of renal failure (drowsiness, vomiting, oliguria), which passed off. At the time of the phloridzin test the patient shewed no signs of renal failure, but he was flabby and unhealthy looking, and there was some thirst. The urea varied from 1.9 to 2.2 per cent. (*see* Chart 25, page 142).

In a third case (Mrs. B.) a uretero-vaginal fistula had followed an extensive operation for carcinoma of the cervix uteri, and necessitated the removal of the left kidney. I was asked to see her by the surgeon in charge on account of œdema of the face and legs and a diminished secretion of urine, the symptoms having set in suddenly 3 months after nephrectomy. The right kidney was enlarged and tender, and there was thickening on the right side of the vaginal vault which had led to the diagnosis of hydronephrosis from recurrence of the pelvic growth. There were 24 ounces of urine in 24 hours containing a trace of albumin and .6 per cent. of urea. No glycosuria followed the injection of 5 mgr. phloridzin. I diagnosed nephritis in a hypertrophied kidney and opposed operative interference. The patient died 14 days later after 7 days of complete anuria, and the *post-mortem* examination confirmed my diagnosis.

Delay in the commencement of glycosuria was observed in some cases on the side of the diseased kidney, but this was not constant. When the quantity of sugar eliminated in these cases was diminished there was a shortened period of glycosuria.

There were some cases where variation in the glycosuria was not to be explained by disease of the kidney. Phloridzin failed to produce glycosuria on one side, while it appeared in much reduced quantity on the other, in two cases where there was insufficient cause for the absence of the sugar. In one, a case of right movable kidney, the supposed healthy kidney eliminated no sugar, while the movable kidney produced only 0.037 gramme. In another, a very nervous man who suffered from attacks of left renal colic and had a history of hæmaturia, the painful kidney eliminated 0.46 gramme of sugar, and the supposed healthy kidney none at all.

Clinical value of the phloridzin test.—As a means of demonstrating the diseased side the phloridzin test is frequently more delicate than other methods.

In the majority of cases in which I have used this method as a test of the functional activity of the kidney, the result has proved reliable when tested by other methods or by operation. The short duration of the glycosuria is an undoubted advantage where the comparative work of the kidneys is under examination. I have seldom required to prolong the examination beyond two hours in order to complete the phloridzin test, and a patient will submit to this duration of ureteric catheterisation without inconvenience. In order to complete the methylene blue test, on the other hand, a much more prolonged catheterisation is necessary, and the same is true with regard to chemical examination of the urine. When the phloridzin test is combined with an artificial polyuria, such as may be produced by drinking hot Contrexéville water or tea, or by taking thiocin (gr. vi. in cachet), it forms, I believe, the most valuable method of estimating the function of one kidney.

There are certain fallacies of the method to which I have already referred. It is difficult to explain the variation of the glycosuria in some apparently healthy kidneys, and its complete absence on more than one occasion where no disease of the kidney could be ascertained. Several causes may be at work in such cases. It is possible that in some the introduction of the catheter into the urethra or ureter may reflexly affect the glucose-forming power of the kidneys. The solution of phloridzin must be freshly prepared, or it soon passes out of solution and forms a cloud of crystals; or it changes in composition, and a brown liquid is produced which is less potent than the fresh solution, and may even fail altogether to produce glycosuria.

It is also necessary to use a reliable preparation of phloridzin, for, as Rothschild * has shewn, an inferior preparation may fail altogether to produce glycosuria in a kidney which is healthy and gives sugar after the

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* *Med. Klin.*, Berlin, 1906.

injection of another preparation. It must be remembered also that a severe degree of renal disease may exist without giving rise to signs which are recognisable by the ordinary clinical methods, but which may yet profoundly affect the elimination of sugar after an injection of phloridzin. Two cases of this nature have been referred to by Achard and Delamere.* The patients suffered from carcinoma of the stomach, and the urine was free from albumin. Injection of phloridzin failed to produce glycosuria, and *post mortem* there was advanced interstitial nephritis in both cases.

The case, to which I have referred, of solitary kidney remaining after nephrectomy for pyonephrosis is a further illustration of this point. The signs of renal failure in this case were practically wanting at the time that the phloridzin test failed to produce glycosuria. But it was known that on two previous occasions the patient had nearly succumbed to failure of the function of this kidney after operation upon its more seriously diseased neighbour.

A disadvantage of the phloridzin method is that it is very sensitive to slight changes in the kidneys, and an exaggerated idea of the extent of the disease may be obtained by studying the glycosuria produced. Larger doses than those in use are more accurate, for there is less possibility of a total absence of glycosuria in slight lesions.

Albarran's experimental polyuria test.—Albarran has established two general rules :—

1. A diseased kidney has a more uniform function than a healthy kidney, and its function varies less from one moment to another the more extensively its parenchyma is destroyed.

2. If one kidney alone is diseased, or is the more diseased of the two, when the urinary function becomes disturbed it modifies its function less than the other.

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* Soc. Biolog., I., 21, 1899.

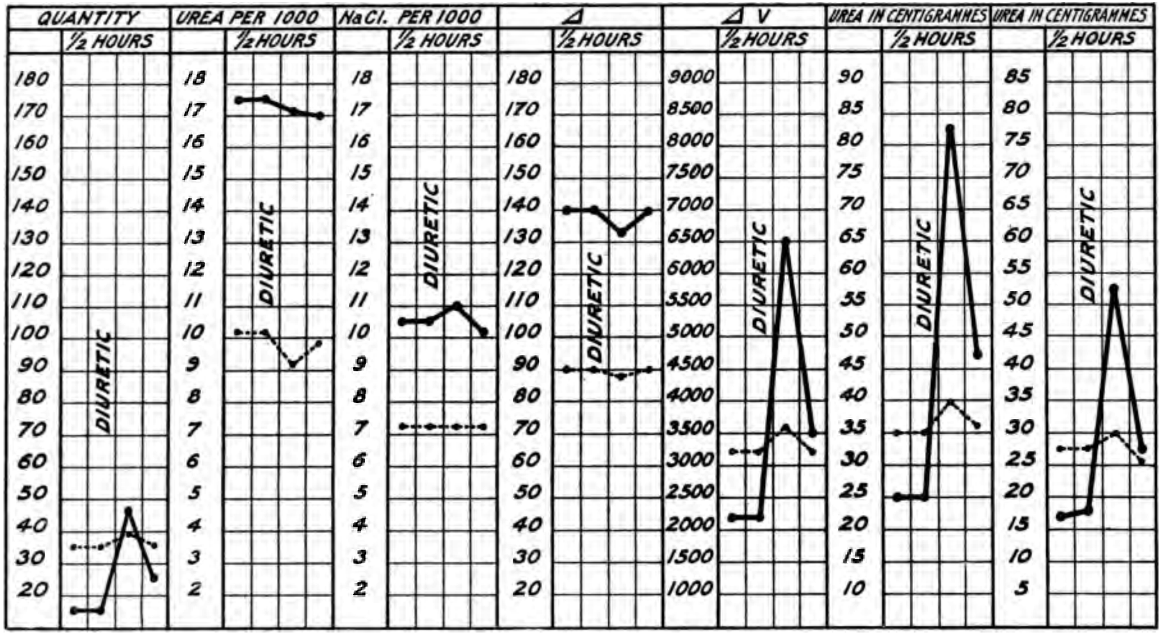

Chart 32 —Albarran's experimental polyuria test. Dotted line shews work of diseased kidney, continuous line that of healthy kidney.

Thus, the diseased kidney is working at its utmost capacity, and has a constant output of low value, while the function of the healthy kidney varies within wide limits. Albarran looks upon the examination of the course of the renal activity as a valuable indication of the functional power of the kidney.

He tests it in the following manner: The patient is given 400 to 600 c.c. of Evian water, both ureters are catheterised, and the urine is collected and examined every half-hour for three hours. The following points are noted for comparison: the quantity of urine, the freezing point (△), the freezing point corrected for volume (△ v), the amount of urea and sodium chloride per litre and in centigrammes, and the phloridzin glycosuria per litre and in centigrammes (Chart 32). In healthy kidneys the quantity of urine should commence to rise in the first half-hour, and reach its highest point in the third half-hour, sinking from the fourth half-hour onwards. During this diuresis the molecular concentration falls, and the percentages of urea, sodium chloride, and sugar are lowered. The absolute quantities of these bodies may rise or may be diminished. On the other hand, a diseased kidney will shew little change in its secretion after drinking mineral water, and the more advanced the destruction of the parenchyma the less will be the variation. One may consider satisfactory the elimination by one kidney of 1.20 grammes to 1.80 grammes of urea during the two hours of the test. The elimination of 75 centigrammes to 1 gramme should be considered as moderate, and anything below these figures as a badly performed function. In feeble women the normal figure is often 90 centigrammes to 1 gramme, and Albarran has seen two emaciated tuberculous subjects in whom the healthy kidney only gave 52 and 86 centigrammes during two hours of the test. Both these cases had satisfactory reactions by this test, and nephrectomy was successfully performed. The freezing point corrected for volume (△ v) shews as great variations as the quantity of urea. In a man during the two hours of the test one may look upon as good, from 12,000 to 17,000, as moderate, from 8,000 to 10,000, and as bad, below 6,000.

NOTE ON THE PRACTICAL APPLICATION OF THE METHODS OF ESTIMATING THE RENAL FUNCTION

In the preceding pages I have described the types of case in which it is desirable that an endeavour should be made to ascertain the condition of the renal function.

The cases fall into two classes—(1) those in which there is disease of the lower urinary tract on which an operation is proposed, and where secondary disease may be present in the kidneys; and (2) those cases where disease is present in one kidney and operation is proposed, and the second kidney may be absent or diseased.

In disease of the lower urinary tract the symptoms of renal inadequacy should be carefully sought for and the kidneys examined by palpation. The examination of the urine may be of assistance, but evidence of renal disease in the urine is frequently masked by the addition of pus or other foreign matter in the bladder.

Either the methylene blue test or the phloridzin test should be carried out. I employ the former, since the prolonged duration of the test is not a disadvantage here as it is in the testing of one kidney. It is difficult on account of the blue colour to carry out both tests concurrently if Fehling's solution is used for the estimation, but they may be used separately. With these tests, and a careful review of the symptoms, there is little danger of overlooking an inadequate renal function.

In cases where one kidney is diseased and it is proposed to perform an operation upon it, general symptoms of renal failure should be carefully sought. The condition of the urine will give little information. The second kidney should be examined by palpation, and, if the case be one of stone, by the X-rays. Cystoscopy and a minute inspection of the ureteric orifices and the efflux will follow, and the ureters should be catheterised. Some urine is collected from each kidney for examination, and then the phloridzin test carried out. A diuretic should be given at the commencement of the test, and the urine collected every quarter of an hour or every half-hour for two or three hours, depending upon the duration of the glycosuria.

The actual quantity and percentage of the urea and sugar are estimated in each sample, and a chart constructed shewing the course of the elimination. By these means the presence of a second kidney is proved, and a very accurate idea of its functional activity at the time of the examination is obtained.

CHAPTER VII

FALLACIES IN THE METHODS OF ASCERTAINING THE FUNCTIONAL ACTIVITY OF THE KIDNEYS

Greater Accuracy of Recent Methods — Partial Activity of the Kidneys in Health — Difference between Ordinary and Potential Activity—Temporary and Permanent Depression of Function—Hypertrophy

MECHANICAL imperfections in the instruments used for the collection of the urine from each kidney have already been discussed, and the possibility that the renal function may be modified by the manipulation necessary in these methods has also been referred to in the foregoing pages. These, therefore, require no further consideration.

In criticism of the more recent methods, it may be urged that the normal function of the kidneys is not to excrete methylene blue or other dyes, or to manufacture sugar under the influence of phloridzin. It is certain, however, that a close parallelism exists between the appearance of these substances in the urine after injection and the secretion of the various urinary constituents. An advantage of the more recently introduced methods is that greater accuracy may be expected from them. The quantity of methylene blue introduced into the circulation is known, and a definite result may be expected from it in a certain time. In regard to the chief urinary constituents, on the other hand, the supply provided to the kidney for elimination is variable, since it depends upon the activity of other organs and on extrarenal factors which are beyond the control of the observer. Further, the duration of the examination in some of the recently introduced methods is short, which is an important advantage where separation of the urines is necessary.

Apart from these fallacies and objections, however, there are others which intimately concern the renal function in health and disease.

1. One of these is *the partial activity of the kidneys in health.* The renal function is not in full activity at any one time under ordinary conditions. Proof of this is to be found in the observation that if the urines of the two kidneys be collected separately and compared, it will be found that one kidney is working more actively than the other, while at another time the kidney which was less active at the first examination is now working with greater energy. Yet if the urines are collected over a sufficiently long period of time, the work of the two will be found approximately equal. At any time during the examination, therefore, some part of one kidney was inactive, or perhaps the whole was working at low pressure.

It may be further stated that the kidney which is for the time working more actively is capable of still greater energy, for, if one kidney be removed without any opportunity for hypertrophy being given to the remaining organ, the latter is quite capable (if healthy) of at once assuming the function which was previously divided between the two organs.

This may be more simply stated as follows:* The functional activity of the two kidneys under ordinary conditions may be represented at one time as—

Right kidney.		*Left kidney.*		*Total.*
3	+	2	=	5

and at another as—

Right kidney.		*Left kidney.*		*Total.*
2	+	3	=	5

---

* The figures given here are not in any way intended to represent the true ratios of potential or actual renal activity, but only to simplify the preceding statements.

The function of the most active kidney may still further increase, if greater demands are made upon it, say to 5 (since one kidney may assume the function of both), and, as each kidney may in turn be shewn to be the more energetic, the potential renal function will amount to--

Right kidney.		*Left kidney.*		*Total.*
5	+	5	=	10

This leaves a difference of 5 between the ordinary activity and the functional activity that may be called forth in exceptional circumstances—the potential activity.

This difference forms a margin of safety which provides against sudden reduction of the secreting tissue by any means, and upon this safety margin the individual depends in the interval between the sudden destruction or removal of a part of the renal tissue and the development of hypertrophy which will replace it.

What this safety margin of renal parenchyma may be if set out in quantities of renal tissue it is not easy to say. It is certain that one-half of the total potential renal function (5 in the preceding figures) is sufficient for the needs of the body, for one kidney may be injured by violence and be removed and the patient shew no signs of an insufficient renal function. How much further the quantity of renal tissue may be reduced and sufficient parenchyma remain to continue an efficient renal function is a matter of some importance. Professor Tuffier* and Dr. J. Rose Bradford† have each endeavoured to answer this question by experiments on animals. The former observer states that the minimal amount of kidney tissue that is compatible with life is gramme to 1.50 grammes of secreting parenchyma for every kilogramme of body weight. The latter investigator has shewn that two-thirds of the total kidney tissue may be removed and the animal remain in good health;

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* "Études expérimentales sur la chirurgie du rein," 1889.

† Proc. of the Roy. Soc., London, 1892.

but if the quantity of renal tissue be reduced to one-quarter, death occurs after an interval.

It may be said, therefore, that the safety margin expressed in quantity of renal tissue is something between $\frac{1}{2}$ and $\frac{2}{3}$ of the total renal tissue, and that this amount may be removed and an adequate renal function be maintained.

It is this margin of safety, this difference between potential and actual renal activity, that introduces a fallacy into the methods of estimating the renal function. An accurate estimation of the renal function in a case of disease of the kidneys might appear to shew a sufficient activity, and yet the disease might have destroyed much or all of the safety margin of renal tissue. An operation such as nephrectomy would reveal the fact that the patient had been living upon the minimum of kidney tissue, and even a temporary interference with its action may be sufficient to overturn the balance and cause death from renal failure.

Although it is apparently beyond the range of practical surgery at the present time to estimate the potential renal activity, yet some approach to it might be made by the coincident use of diuretic drugs with the recent methods of estimating the renal function.

2. Another fallacy is the *temporary reduction of function* that may be brought about by reflex or other influences. It is impossible, on examining a patient, to distinguish between temporary depression of function and permanent reduction of function.

This temporary depression of function may be observed in disease of the lower urinary tract and also in disease of one kidney.

The obstruction of an enlarged prostate produces a reduction in the renal function that is partly temporary and partly permanent. The temporary depression of the renal function is due to the existing obstruction, and the permanent reduction of function to interstitial changes in the kidney brought about by the obstruction, or to destruction of kidney tissue by septic inflammation. The removal of the obstruction, in such a case, will be followed by an improvement in the renal function which cannot be measured beforehand. Yet upon this improvement may depend the progress of the patient after he has survived the removal of the obstruction.

Suprapubic cystotomy and drainage of the bladder in a case of prostatic obstruction, where the condition of the patient from renal inadequacy is such as to preclude the removal of the prostate, is frequently followed by so pronounced an improvement in the renal activity that a prostatectomy may be performed with success. (*See* the case of G. B., page 110.)

Again, in the case of disease of one kidney the function of the second kidney may suffer depression from changes in its substance, such as waxy disease or a similar disease to that in the first kidney, but less advanced. But the depression of the function of the second kidney may be partly or even wholly due to reflex influences passing from its diseased neighbour. This renorenal reflex has been discussed in the preceding pages. The removal of the diseased kidney, or the source of irritation in it, may be followed by a striking improvement in the function of the healthy or slightly diseased kidney (*see* Chart 7, page 43; and Chart 8, facing page 46). There is no means by which it is possible to ascertain how much the depression of function may be due to such temporary influences, and how much to actual destruction of renal parenchyma.

3. Further, it is impossible to judge before operation *how far hypertrophy will compensate for the reduction of kidney tissue.* Professor Tuffier studied this question by experiments on animals, and concluded that compensatory hypertrophy only takes place when the kidney is partly or wholly normal. If it is the seat of parenchymatous

nephritis the hypertrophy fails. According to this observer, the quantity of renal parenchyma necessary to maintain life is equal to almost a quarter of the weight of the entire kidney tissue. A portion of kidney tissue equal to this weight suffices to reconstruct, by compensatory hypertrophy, a quantity of parenchyma equal in weight to one entire kidney.

In the human subject, where one kidney is completely destroyed by disease, it may be accepted that the remaining kidney has hypertrophied to its full capacity, and if this second organ is considered inadequate to continue the renal function after operation, no further help need be expected from hypertrophy. But in judging the gravity of a reduction of the renal function in cases where the disease has partly destroyed one kidney and the second organ is the seat of less advanced disease, the possibility of an improvement in the function of the second kidney from hypertrophy after nephrectomy has been performed must be taken into consideration. A case recorded by Mr. Henry Morris* is of interest in this relation. In a woman aged 20 years, whose right kidney had been removed by another surgeon for tuberculous disease four years previously, he excised a tuberculous nodule, involving about one-third of the left kidney. Seven years later the remaining portion of the kidney was explored and a quantity of pus evacuated. The patient died four and a half months later from acute tuberculosis of the lungs. Only two-thirds of one kidney existed, and this remaining piece was very extensively fibrosed, so that the actual amount of secreting tissue must have been very small indeed.

These fallacies have been dealt with at some length, for they must arise for consideration where any attempt is made to estimate the function of the kidneys in view of operation upon a case of surgical disease of these organs.

* *Arch. of the Middlesex Hosp.*, Vol. vi., p. 1.

But although they complicate the whole question of the estimation of the renal function, they do not detract from the value of the methods that have been discussed in the preceding pages, nor do they absolve the surgeon from an attempt to form an accurate estimate of the activity of the kidneys, not only in the case where operation is proposed upon one of these organs, but also where surgical interference is to be undertaken in diseases of the lower urinary tract.

APPENDIX

CASES OF DEATH FROM ANURIA AND URÆMIA IMMEDIATELY FOLLOWING OPERATIONS UPON THE KIDNEY

No.	*Operator or Recorder.*	*Reference.*	*Condition of Operated Kidney.*	*Operation.*	*Condition of Second Kidney.*
1	König-Pels	*Deut. Zeitschr. f. Chir.*, 1900, lv., 9	Tuberculous disease	Nephrectomy	Obsolete tuberculous disease.
2	Pinner	*Arch. f. klin. Chir.*, 1898, 447	Tuberculous disease	Nephrectomy	Tuberculous pyonephrosis.
3	Duncan	*Edinburgh Med. Jour.*, i., 1881	Tuberculous disease	Nephrotomy	Amyloid disease.
4	Jowers	*Lancet*, 1884, i., p. 13	Tuberculous disease	Abdominal nephrectomy	No post-mortem examination.
5	Bennett May	*Brit. Med. Jour.*, 1883, ii., p. 438	Tuberculous disease	Nephrectomy	A mass of tuberculous caseous material.
6	Morris	Hunterian Lectures, 1898	Perinephritic abscess and tuberculous disease	Nephrectomy	Tuberculous disease.
7	Morris	Hunterian Lectures, 1898	Tuberculous disease	Nephrectomy	Fatty degeneration.
8	Israel	"Nierenkrankheiten," 1901	Tuberculous disease	Nephrectomy	Tuberculous nodule and chronic parenchymatous nephritis.
9	Israel	Idem	Tuberculous disease	Nephrectomy	Parenchymatous and interstitial nephritis.
10	Israel	Idem	Tuberculous disease	Nephrotomy	Amyloid degeneration.
11	Steinthal	*Münch. med. Woch.*, 1896, 16	Tuberculous disease	Nephrectomy	Sac with clear fluid.
12	Verhoogen	*Ann. de la Soc. Belge de Chirurgie*, 1898, vi., 246	Tuberculous disease	Nephrotomy	Absent.
13	Casper	"Handb. der Cystoskopie," 1898	Tuberculous disease	Nephrectomy	Absent.
14	Gardner	*Australian Med. Jour.*, Apr. 15, 1885	Tuberculous disease	Nephrotomy	Tuberculous disease.

No.	*Operator or Recorder.*	*Reference.*	*Condition of Operated Kidney.*	*Operation.*	*Condition of Second Kidney.*
15	O'Reilly	*Brit. Med. Jour.*, 1885, i., 428	Tuberculous disease	Nephrectomy	No post-mortem examination.
16	Barwell	*Brit. Med. Jour.*, 1881, i., 642	Tuberculous disease	Nephrectomy	Not stated.
17	Swain	*Lancet*, May 21, 1892, p. 1132	Tuberculous disease	Nephrectomy	Tuberculous disease.
18	Belfield	*N.Y. Med. Rec.*, May 14, 1887, p. 537	Tuberculous disease	Nephrotomy	Tuberculous disease.
19	Riedel	"Erfahrungen über die Gallensteinkrankheit," Berlin, 1892, p. 50; quoted by Facklam, *Archiv. f. klin. Chir.*, 1893, p. 715	Tuberculous disease	Nephrectomy	Tuberculous disease.
20	Monod	*Ann. d. malad. d. org. génito-urin.*, 1889, vii., p. 649	Tuberculous disease	Nephrectomy	Tuberculous disease.
21	Doyen	*La semaine méd.*, 1889, p. 295	Tuberculous disease	Nephrectomy	Amyloid degeneration.
22	Doyen	Idem	Tuberculous disease	Nephrectomy	Amyloid degeneration.
23	Schede	"Erfahrungen über Nieren-extirpation," Hamburg, 1890, No. 1	Tuberculous disease	Nephrectomy	Tuberculous disease.
24	Wright	*Brit. Med. Jour.*, 1885, i., 432	Tuberculous disease	Nephrectomy	Tuberculous disease.
25	Brewer	*N.Y. Med. Rec.*, Feb. 18, 1905	Tuberculous disease	Nephrotomy	No autopsy.
26	Brewer	Idem	Tuberculous disease	Nephrotomy	No autopsy.
27	Peters	*N.Y. Med. Jour.*, Nov., 1872	Tuberculous disease	Nephrectomy	Tuberculous disease.
28	Sendler	*Münch. med. Woch.*, No. 5, 1899, p. 137	Tuberculous disease	Nephrectomy	Cyst with thin atheromatous walls.
29	Sonnenberg	*Berl. klin. Woch.*, 1884, No. xlvii.	Calculous pyelonephritis	Nephrectomy	Hypertrophy and fatty degeneration.
30	Wantscher	Inaug. Diss., quoted by Casper, "Nierendiagnostik," 1901	Calculous disease	Nephrotomy	Calculus. Kidney destroyed.
31	Albertin	*Ann. d. malad. d. org. génito-urin.*, 1898, iv.	Calculous disease	Nephrotomy	Calculous disease.
32	Litten	*Berl. klin. Woch.*, Oct. 31, 1898, p. 983	Calculous disease	Nephrectomy	Calculous disease.

No	*Operator or Recorder.*	*Reference.*	*Condition of Operated Kidney.*	*Operation.*	*Condition of Second Kidney.*
33	Amray	Soc. anat. d. Paris, 14, June, 1899	Calculous disease	Nephrotomy	Calculous hydronephrosis.
34	Parker	*Lancet*, i., 1887, 625	Calculous disease	Nephrolithotomy	"Both kidneys diseased."
35	Cullingworth	*Trans. Path. Soc. Lond.*, Vol. xxxvi.	Calculous disease	Abdominal nephrolithotomy	Calculus in ureter.
36	Duncan	Newman, "Surgical Diseases of the Kidney," 1888	Calculous disease	Nephrolithotomy	Hydronephrosis, stone in ureter.
37	Lange	*N.Y. Med. Rec.*, No. 6, Aug., 1880	Calculous pyonephrosis	Nephrectomy	Degenerated, cystic; pelvis and ureter obliterated.
38	Küster	*Deut. med. Woch.*, 1888, xxi., 418	Calculous hydronephrosis	Nephrotomy for stone	Hydronephrosis.
39	Herczel	*Beitr. z. klin. Chir.*, 1890, vi., 489	Calculous disease	Nephrotomy	Amyloid disease.
40	Herczel	Idem	Calculous disease	Nephrotomy	Atrophic and calculi.
41	Hildebrand	*Deut. Zeitschr. f. Chir.*, 1895, 97	Calculous hydronephrosis	Nephrectomy	Hydronephrosis.
42	Morris	Hunterian Lectures, 1898	Calculous disease	Nephrotomy for stone	Calculous kidney and stone in ureter.
43	Morris	Idem	Calculous disease	Nephrotomy for stone	Small atrophied.
44	Morris	Idem	Calculous disease	Nephrotomy for stone	Not stated.
45	Morris	Idem	Calculous disease	Nephrotomy for stone	No post-mortem examination.
46	Morris	Idem and *Brit. Med. Jour.*, 1892, i., 1065, and 1893, i., p. 4	Calculous disease	Nephrectomy	Interstitial nephritis.
47	Morris	Hunterian Lectures, 1898	Calculous disease	Nephrectomy	Calculous pyonephrosis.
48	Morris	Hunterian Lectures, 1898	Fistula, previous calculi	Nephrectomy	Not stated.
49	Thomas	*Brit. Med. Jour.*, July 2, 1904	Calculous disease	Nephrectomy	Atrophy.
50	Langley Browne	*Brit. Med. Jour.*, 1886, May 1, p. 820	Calculous disease	Nephrectomy	Atrophied cystic kidney.
51	Morris	Hunterian Lectures, 1898	Calculous disease	Nephrolithotomy	Fatty degeneration.
52	Morris	*Trans. Clin. Soc.*, Vol. xx., p. 106	Calculous disease	Nephrotomy for stone	Calculous pyonephrosis.
53	Kümmel	*Beitr. z. klin. Chir.*, 1903, xxxvii., S. 788	Calculous pyonephrosis	Nephrectomy	Calculous pyonephrosis.

No.	*Operator or Recorder.*	*Reference.*	*Condition of Operated Kidney.*	*Operation.*	*Condition of Second Kidney.*
54	Péan	Brodeur, "Affections du Rein," 1886	Pyonephrosis	Nephrectomy	No post-mortem examination.
55	Israel	"Nierenkrankheiten," 1901	Pyonephrosis	Nephrectomy	Suppurative pyelonephritis.
56	Renton	Newman, "Surgical Diseases of the Kidney," 1888	Pyonephrosis	Nephrotomy	Abscess.
57	Herczel	Loc. cit.	Pyonephrosis	Nephrectomy	Cystic and waxy.
58	Herczel	Loc. cit.	Pyonephrosis	Nephrectomy	Pyonephrosis.
59	Morris	Hunterian Lectures, 1898	Pyonephrosis	Nephrectomy	Hydronephrosis.
60	Morris	Idem	Pyonephrosis	Nephrectomy	No post-mortem examination.
61	Kümmel	Loc. cit.	Pyonephrosis	Nephrectomy	Pyonephrosis.
62	Hildebrand	*Deut. Zeitschr. f. Chir.*, B. 40	Pyonephrosis	Nephrectomy	Necrosis of renal epithelium.
63	Czerny	*Deut. med. Woch.*, 1881, No. xxxii.	Hydronephrosis	Nephrectomy	Atrophied, pelvis obliterated.
64	Lotheison	*Arch. f. klin. Chir.*, 1896, 731	Hydronephrosis	Nephrotomy	Fatty degeneration and parenchymatous nephritis.
65	Israel	"Nierenkrankheiten," 1901	Hydronephrosis	Nephrectomy	Granular kidney and slight dilatation.
66	Herczel	*Beitr. z. klin. Chir.*, 1890, vi., 489	Hydronephrosis	Nephrectomy	Completely atrophic.
67	Schetelig	*Arch. f. Gynaek.*, *Rev. Sc. Med.*, 1873, 974	Hydronephrosis	Nephrectomy	Absent.
68	Guth	*Ver. Bl. d. pfälz. Aerzte*, 1893; quoted by Graser, *Deut. Archiv. f. klin. Med.*, B. 55, 1895	Hydronephrosis	Nephrectomy	Absent.
69	Terrier	Brodeur, "Affections du rein," 1886	Carcinoma	Nephrectomy	Secondary nodules.
70	Lotheison	*Arch. f. klin. Chir.*, 1896, 731	Carcinoma	Nephrectomy	Nodules of carcinoma.
71	Benecke	*Berl. klin. Woch.*, 1897, 84	Growth	Nephrectomy	Hydronephrosis
72	von Bergmann	Bolz. Dissert. Dorpat, 1883, p. 33, quoted by Newman, "Surgical Diseases of the Kidney," 1888	Sarcoma	Nephrectomy	Not stated.

No.	*Operator or Recorder.*	*Reference.*	*Condition of Operated Kidney.*	*Operation.*	*Condition of Second Kidney.*
73	Chiene	Quoted by Newman, "Surgical Diseases of the Kidney," 1888	Growth	Nephrectomy	Not stated.
74	Lüche	*Deut. Zeitschr. f. Chir.*, 1881., xv., 519	Carcinoma	Nephrectomy	Shrunken and cystic.
75	Israel	"Nierenkrankheiten," 1901	Suppurative pyelonephritis	Nephrotomy	Suppurative pyelonephritis.
76	Elder	*Lancet*, Aug., 1885, p. 196	Suppurative pyelonephritis	Nephrectomy	Fatty degeneration.
77	Gardner	*Australian Med. Jour.*, April 15, 1885	Suppurative pyelonephritis	Nephrectomy	Fatty degeneration.
78	von Bergmann	*Berl. klin. Woch.* 1885, No. 48	Pyelonephritis and perinephritic abscess	Nephrectomy	Pyelonephritis.
79	Sadler	*Lancet*, i., 1886, p. 919	Suppurating kidney	Nephrotomy	Not stated.
80	Buss	*Zeitschr. f. klin. Med.*, B. 38, H. 4, 5, 6	Displaced kidney	Nephrectomy	Absent.
81	Ferrier	Quoted by Brodeur, "Affections du rein," 1888	Floating kidney	Nephrectomy	Hydronephrosis.
82	Merckel	*Bayer aerztl. Intell.*, 1879, xxi.	Movable dilated kidney	Nephrectomy	Fatty degeneration.
83	Polk	*N.Y. Med. Jour.*, Feb. 17, 1883, and *Lancet*, Mar. 24, 1883, p. 514	Painful floating kidney	Nephrectomy	Absent.
84	Lindner	"Uber die Wanderniere bei Frauen Neuwied," 1888; quoted by Graser, *Deut. Archiv. f. klin. Med.*, B. 55, 1895	Floating kidney	Nephrectomy	Absent.
85	Jowers	*Lancet*, Jan. 5, 1884	Cyst	Nephrectomy	No autopsy.
86	Hildebrand	*Deut. Zeitschr. f. Chir.*, 1895, xcvii.	Cystic	Nephrotomy	Cystic.
87	Billon	*Ann. d. malad. d. org. génito-urin.*, 1905, No. 23, p. 124	Polycystic	Nephrectomy	Polycystic.

No.	*Operator or Recorder.*	*Reference.*	*Condition of Operated Kidney.*	*Operation.*	*Condition of Second Kidney.*
88	Winter	*Arch. f. klin. Chir.*, lxix., 1903, p. 611	Cystic	Nephrectomy	Absent.
89	Houzell	*Rev. de Chir.*, 1898, 692	Hydatid cyst	Nephrectomy	Absent.
90	Weir	*Med. News*, 1898	Traumatic abscess	Nephrotomy	Interstitial nephritis.
91	Mareille	Soc. Anat., 14, June, 1899	Diffuse nephritis	Nephrotomy	Atrophy, calculus.
92	Morris	Hunterian Lectures, 1898	Healthy	Nephrotomy	Tuberculous disease.
93	Lotheison	*Arch. f. klin. Chir.*, 1896, 731	Ureteric fistula	Nephrectomy	Parenchymatous nephritis.
94	Schulz	Quoted by Casper, " Handb. d. Cystoskopie "	Not stated	Nephrectomy	Abscess.
95	Schuchardt	*Aerzt. Bericht. über das Stadt Krankenhaus in Stettin*, 1890, xci.; *Beitr. z. Centralbl. f. Chir.*, 1891, No. xxvi., p. 142	Large fluctuating tumour	Nephrectomy	Not stated.

INDEX

Age, influence on anuria, 48
Albarran catheter cystoscope, 194
—— experimental polyuria test, 252
Anuria, causes of, 45
——, obstructive, 2, 7, 8, 10, 17
——, reflex causes of, 46
Azotised products, elimination of, 34

Balthazard's method of estimation of chlorides, 63
Beckmann's cryoscopic apparatus, 55
Bernard's method of renal exploration, 64
Bladder, carcinoma of, 7
——, condition of, in renal inadequacy, 18
——, spasm of, in catheterisation, 204
——, washing out the, 204
——, *see also* Cystitis
Blood, cryoscopy of, 53, 67, 70
——, electrical resistance of, 78
——, state of, during elimination of methylene blue, 98
Blue, *see* Methylene blue
Bright's disease, renal elimination in, 83

Calculus, renal, 45, 152
——, ——, bilateral, 16
——, ——, elimination of blue in, 112
——, ——, —— of sugar in, 244
——, ——, —— of blue absent in, 115
——, vesical, 28
Carcinoma of bladder, 7
Carmine, *see* Indigo-carmine
Cases, 6, 9, 11, 14, 16, 28, 44, 97, 152, 162, 167, 227, 237, 245, 247, 249
Casper catheter cystoscope, 193
Cathelin separator, 186
Catheter cystoscope, Albarran, 193
—— ——, Casper, 192
—— ——, Freudenberg, 195, 207
—— ——, Nitze, 191, 200
—— "occlusion," 197
——, ureteral, 196
Catheterisation, effect of, on secretion of urine, 225
——, pyelonephritis following, 11
——, ureteral, 241
——, ——, duration of, in phloridzin test, 251
——, ——, fallacies and difficulties of, 212
——, ——, operation of, 203
Chlorides, estimation of, 59, 63, 232
—— in urine, 36
——, secretion of, by each kidney, 225
Chromocystoscopy, 174, 241
Chromogen, elimination of, 101
——, identity of, 102
——, testing for, 87
Claude's method of estimation of chlorides, 61, 65
Clinical examination, 146
Colic, renal, glycosuria in, 137
Congenital malformation of ureters, 166
Corpuscles, red, suspension of, 73
Cryoscopy of blood and urine, 53, 57, 70
Cystic disease, renal, 152

Cystitis, effect of ureteral catheterisation in, 217
——, injection of blue in, 107
——, washing bladder in, 204
Cystoscope, catheter, Albarran, 193
——, ——, Casper, 192
——, ——, Freudenberg, 195, 207
——, ——, Nitze, 200
——, sterilisation of, 199
——, use of, in renal surgery, 1
Cystoscopy, difficulties of, 213
—— of ureteric openings, 159, 161
Cystotomy, 13

Delirium in renal disease, 23
Deposits, urinary, 58
Diagnosis of renal failure, 149
Diuretics, influence of, on renal secretion, 131
Donnan's apparatus for measuring surface tension, 80
Dysphagia in renal disease, 20

Efficiency, renal, *see* Function
Electrical resistance of the blood and urine, 75
Elimination of substances by the kidneys, 83, 90
Emaciation in renal disease, 21
Estimation of urea, sodium chloride, and phosphates, 232
—— of total renal function, 1

Fallacies in methods of examination, 251
Formalin sterilisers, 199
Freezing point of blood and urine, 53, 70
Freudenberg catheter cystoscope, 195, 207
Function, renal, catheterisation of ureters and, 203
——, ——, elimination of substances by kidney, 83
——, ——, estimation of total, 1
——, ——, examination of urine, 32
——, ——, fallacies in methods of ascertaining, 251
——, ——, glandular, 129
Function, renal, symptoms of failure of, 6
——, ——, ——, general, 2
——, ——, ——, local signs of, 27
——, ——, testing urine of each kidney, 223, 255

Glandular function of the kidney, 129
Glycosuria in renal disease, 137, 144
—— of normal kidneys, 133
——, phloridzin test for each kidney, 242
——, *see also* Sugar

Hæmolysis, method of obtaining, 74
Headache in renal disease, 21
Hiccough in renal disease, 22
Hippuric acid, elimination of, 129
Hydronephrosis, 27
——, cause of oliguria, 46
——, calculous, elimination of sugar in, 247
——, effect of, on secretion of urine, 227
——, elimination of blue in, 114, 234
Hyperglycosuria and hypoglycosuria, 134
Hypertrophy, renal, compensatory, 149

Indigo-carmine test, 120
—— —— for each kidney, 241
Infection, danger of, in ureteral catheterisation, 216, 220
Instruments, sterilisation of, 199
Iodide of potassium, elimination of, 122

Kelly's speculum for direct ureteral catheterisation, 209
—— ureteral searcher, 211
Kidneys, diseases of, normal elimination of sugar in, 136
——, ——, primary, elimination of blue in, 111
——, ——, secretion of urine by, 227

Kidneys, elimination of substances by, 84, 90
——, examination of, 27
——, exposure of, 30
—— as a filter, 52
——, hypertrophy, compensatory, 149
——, operations on, 1, 6, 11
——, *post-mortem* examinations of, 6, 9, 11, 24, 29
——, single, 151
——, ——, displaced, 169
——, *see also* Function and Movable kidney
Kilner's substitute for cryoscopy, 72
Knee-jerks in renal disease, 23
Koranyi's method of estimation of chlorides, 59

Liver, blue and chromogen secreted by, 100
Luys' separator, 182

Malformations in the genital system, 155, 166
Mauté's method of estimation of chlorides, 65
Mental condition in renal disease, 22
Methods of estimating the renal function, 255, 257
Methylene blue, elimination of, delay in, 110
—— ——, ——, negative result in some cases, 114
—— —— test, 30, 84
—— —— ——, technique of, 86
—— —— ——, value of, 118
—— ——, use of, 104, 257
Molecular content of urine, 58
Mortality in renal surgery, 2
Movable kidney, elimination of sugar in, 140, 243
—— ——, estimation of urea in, 233

Nausea in renal disease, 21
Nephrectomy, elimination of blue and chromogen after, 117
Nephrectomy, first performance of, 1
——, increased secretion of urine after, 43
——, normal phloridzin glycosuria after, 141
Nephritis, cause of deficient renal function, 6
——, chlorides in urine in, 36
——, elimination of methylene blue in, 93, 97
Nephropexy, first performance of, 1
Nephrolithiasis, cause of anuria, 45
Nephrolithotomy, first performance of, 1
Nephrotomy, 1, 13
——, fatal result of, 30
Nervous symptoms in renal disease, 22
Nitrogen in urine, 35
Nitze catheter cystoscope, 200

"Occlusion catheter," 197
Œdema in renal failure, 26
Oliguria and polyuria, 41
——, reflex causes of, 46
Operations on the kidney, 1, 6, 11
Osmotic pressure, 54

Pain in renal disease, 19
Phloridzin glycosuria of normal kidneys, 133
—— —— test, 130
—— —— ——, clinical value of, 143, 250
—— —— —— for each kidney, 242
—— —— —— in renal disease, 136
——, injections of, 9
Phosphates, estimation of, 232
Polyuria alternating with oliguria, 41
——, causes of, 37
——, effect of renal disease on, 228
—— following catheterisation, 225
—— test, Albarran's experimental, 252

Post-mortem examinations of kidneys, 6, 9, 11, 24, 29
Potassium, *see* Iodide
Prostate, enlargement of, 12
——, ——, absent elimination of blue in, 116
——, ——, deficient renal function in, 6
——, ——, elimination of methylene blue in, 93
——, ——, impediment to ureteral catheterisation, 213
——, ——, injection of blue in, 108
——, ——, malignant, 14
——, ——, phloridzin glycosuria in, 139
——, ——, polyuria in, 39
——,——, renal symptoms in, 18
Prostatectomy, 15
Pulse in septic pyelonephritis, 26
Pyelonephritis, acute suppurative, 11, 24
——, suppurative, 153
Pyonephrosis, calculous, 43
——, ——, effect of, on secretion of urine, 227
——, ——, elimination of blue in, 114
——, ——, elimination of sugar in, 245
——,——, estimation of urea in, 234
——, no elimination of blue in, 117

Reflex causes of anuria and oliguria, 49
Rigors in septic renal disease, 24
Röntgen rays in diagnosis, 1, 149
Rosaniline test, 121

Salicylate of soda, elimination of, 124
Separation of the two urines, 220
"Separators" for urine, 181
Skin as index to renal disease, 21
Soda, *see* Salicylate
Sodium, *see* Chlorides
Statistics and pathology, renal, 155
Sterilisation of instruments, 199
Stricture, *see* Urethra
Sugar, elimination of, by the kidneys, 130, 243
——, excretion of, absence of, in certain lesions, 144
——,——, drugs that diminish, 133
——, *see also* Glycosuria
Symptoms of failure of renal function, 2, 6, 27, 146
Syphilis, elimination of methylene blue in, 99

Temperature in obstructive anuria, 8, 10
—— in renal disease, 23
—— in septic pyelonephritis, 13
——, sub-normal, in pyelonephritis, 26
Tests for each kidney, 235
—— of glandular function of kidney, 129
—— of urine of both kidneys, 223
——, *see also* Methylene blue and Phloridzin
Thirst in renal disease, 20
Tongue as an index of renal disease, 20
Toxicity of urine, 124
—— ——, determination of, 127
Tuberculosis, renal, 153
——, ——, absence of glycosuria in, 249
——, ——, elimination of blue in, 113
——, ——, estimation of urea in, 233
Tubes for catheters, syringes, etc., 201
Tumours, renal, 151

Urea, estimation of, 232
——, excretion of, quantity, 33
Ureteral searcher, Kelly's, 211
Ureters, catheters for, 196
——, catheterisation of, 241
——, ——, duration of, in phloridzin test, 251
——, ——, effect on secretion of urine, 226

Ureters, congenital malformation of, 166
——, cystoscopy of, 159, 161
——, orifices of, 165
——, ——, pathological changes in, 172
Urethra, stricture of, 9
——, ——, cause of renal inadequacy, 18
——, ——, injection of blue in, 107
——, ——, reduced elimination of sugar, 138
Urethrotomy, internal, 9
Urinary septicæmia, 14, 45
—— ——, condition of the skin in, 21
Urine, analysis of, 7, 9, 58, 246
——, characters of, on each side, 229
——, chemical examination of, 32
——, chlorides in, examination of, 59
——, cryoscopy of, 53, 57, 230
——, efflux of, from ureter, 159
——, electrical resistance of, 75
Urine, examination of, 32
——, quantity of, 37
——, secretion of, 42
——, ——, effect of catheterisation on, 225
——, ——, normal amount of, 224
——, separation of, 176
——, state of, during elimination of methylene blue, 98
——, suppression of, *see* Anuria
——, surface tension of, 80
——, testing, of both kidneys, 225
——, toxicity of, 124
——, ——, determination of, 127
Urines, relative density and tension of, 81
——, separation of, 176, 219
" Urotoxie," Bouchard on, 125

Vomiting in renal disease, 21

Walker (Thomson), ureteral catheter, 198
Wright's substitute for cryoscopy, 72

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